PALM INTRANET

Day : Thursday
Date: 11/8/2007
Time: 16:31:33

Inventor Information for 10/791223

Inventor Name	City	State/Country
EPSTEIN, MEL H.	BRISTOL	RHODE ISLAND
WIIG, KJESTEN A.	PROVIDENCE	RHODE ISLAND
VERHEIJEN, JEROEN	CRANSTON	RHODE ISLAND

Appln Info | Contents | Petition Info | Atty/Agent Info | Continuity/Reexam | Foreign D

Search Another: Application # [ ] Search **or Patent#** [ ] Search

PCT / [ ] / [ ] Search **or PG PUBS #** [ ] Search

Attorney Docket # [ ] Search

Bar Code # [ ] Search

To go back use Back button on your browser toolbar.

Back to PALM | ASSIGNMENT | OASIS | Home page

```
=> file caplus medline biosis embase
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        58.35      58.56

FILE 'CAPLUS' ENTERED AT 16:12:00 ON 08 NOV 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'MEDLINE' ENTERED AT 16:12:00 ON 08 NOV 2007

FILE 'BIOSIS' ENTERED AT 16:12:00 ON 08 NOV 2007
Copyright (c) 2007 The Thomson Corporation

FILE 'EMBASE' ENTERED AT 16:12:00 ON 08 NOV 2007
Copyright (c) 2007 Elsevier B.V. All rights reserved.

=> s alzheimer or dementia or (senile (1) dementia) or alzheimer? or (memory (s)
loss)
L5      338080 ALZHEIMER OR DEMENTIA OR (SENILE (L) DEMENTIA) OR ALZHEIMER? OR
               (MEMORY (S) LOSS)

=> s l5 or ((mild (1) cognitive) or forgetfulness)
L6      346406 L5 OR ((MILD (L) COGNITIVE) OR FORGETFULNESS)

=> s l6 and (300-62-9/rn or amphetamine or amfetamine or methylphenthylamine or
desoxynorephedrine or menylisopropylamine or methylbenzenethanamine or
aminopropylbenzene)
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
L7         734 L6 AND (300-62-9/RN OR AMPHETAMINE OR AMFETAMINE OR METHYLPHENT
               HYLAMINE OR DESOXYNOREPHEDRINE OR MENYLISOPROPYLAMINE OR METHYLB
               ENZENETHANAMINE OR AMINOPROPYLBENZENE)

=> s l6 and (156-34-3/rn or levoamphetamine or l-amphetamine or levamfetamine )
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
L8          18 L6 AND (156-34-3/RN OR LEVOAMPHETAMINE OR L-AMPHETAMINE OR
               LEVAMFETAMINE )

=> s l6 and (methamphetamine or methylamphetamine or deoxyephedrine or
metamfetamine )
L9         259 L6 AND (METHAMPHETAMINE OR METHYLAMPHETAMINE OR DEOXYEPHEDRINE
               OR METAMFETAMINE )

=> s l6 and (33817-09-3/rn or levmetamfetamine or l-methylamphetamine or
l-methamphetamine)
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
L10         13 L6 AND (33817-09-3/RN OR LEVMETAMFETAMINE OR L-METHYLAMPHETAMIN
               E OR L-METHAMPHETAMINE)

=> s l7 and l9
L11         85 L7 AND L9

=> s l8 and l10
L12          4 L8 AND L10

=> s l11 and pd <=2001
```

```
   2 FILES SEARCHED...
L13          25 L11 AND PD <=2001

=>

=> s l11 and pd <=2000
   2 FILES SEARCHED...
L14          22 L11 AND PD <=2000

=> s epstein or wiig or verheijen
L15       83146 EPSTEIN OR WIIG OR VERHEIJEN

=> s l15 and l11
L16           0 L15 AND L11

=> s epstein/au or wiig/au or verheijen/au
L17          10 EPSTEIN/AU OR WIIG/AU OR VERHEIJEN/AU
```

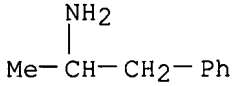
L2 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2007 ACS on STN
RN 300-62-9 REGISTRY
ED Entered STN: 16 Nov 1984
CN Benzeneethanamine, α-methyl- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzeneethanamine, α-methyl-, (±)-
CN Phenethylamine, α-methyl-, (±)- (8CI)
OTHER NAMES:
CN (±)-α-Methylphenethylamine
CN (±)-α-Methylphenylethylamine
CN (±)-β-Phenylisopropylamine
CN (±)-1-Phenyl-2-aminopropane
CN (±)-Desoxynorephedrine
CN (±)-Phenylisopropylamine
CN α-Methyl-β-phenylethylamine
CN α-Methylbenzeneethanamine
CN α-Methylphenethylamine
CN α-Methylphenylethylamine
CN β-Aminopropylbenzene
CN β-Phenylisopropylamine
CN 1-Benzylethylamine
CN 1-Methyl-2-phenylethylamine
CN 1-Phenyl-2-aminopropane
CN 1-Phenyl-2-propanamine
CN 1-Phenyl-2-propylamine
CN 2-Amino-1-phenylpropane
CN 3-Phenyl-2-propylamine
CN Actedron
CN Adderall
CN Adderall XR
CN Adipan
CN Allodene
CN **Amfetamine**
CN **Amphetamine**
CN Anorexine
CN Benzebar
CN Benzedrine
CN Benzolone
CN Desoxynorephedrine
CN dl-α-Methylphenethylamine
CN Elastonon
CN Fenopromin
CN Finam
CN Isoamyne
CN Isomyn
CN Mecodrin
CN Norephedrane
CN Novydrine
CN NSC 27159
CN Obesin
CN Obesine
CN Oktedrin
CN Ortedrine
CN Percomon
CN Phenamine
CN Phenedrine
CN **Racemic Amphetamine**
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DR 60-15-1, 17108-96-2, 96332-84-2
MF C9 H13 N
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS,

BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, DDFU, DETHERM*, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSPATENTS, IPA, MEDLINE, MRCK*, MSDS-OHS, PIRA, PROMT, PS, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, USPATOLD, VETU

(*File contains numerically searchable property data)

Other Sources: DSL**, EINECS**, TSCA**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)



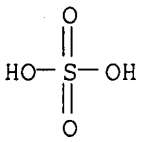
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9324 REFERENCES IN FILE CA (1907 TO DATE)
679 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
9347 REFERENCES IN FILE CAPLUS (1907 TO DATE)
5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L1 ANSWER 502 OF 503 REGISTRY COPYRIGHT 2007 ACS on STN
RN 51-62-7 REGISTRY
ED Entered STN: 16 Nov 1984
CN Benzeneethanamine, α-methyl-, (αR)-, sulfate (2:1) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzeneethanamine, α-methyl-, (R)-, sulfate (2:1)
CN Phenethylamine, α-methyl-, sulfate (2:1), (-)- (8CI)
OTHER NAMES:
CN **(-)-Amphetamine sulfate**
CN **L-Amphetamine sulfate**
CN **l-Amphetamine sulfate**
CN Levedrine
CN NSC 27105
FS STEREOSEARCH
MF C9 H13 N . 1/2 H2 O4 S
LC STN Files: BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, EMBASE, RTECS*, SYNTHLINE, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

CM 1

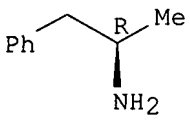
CRN 7664-93-9
CMF H2 O4 S



CM 2

CRN 156-34-3
CMF C9 H13 N

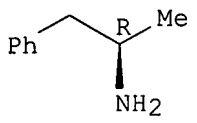
Absolute stereochemistry. Rotation (-).



170 REFERENCES IN FILE CA (1907 TO DATE)
170 REFERENCES IN FILE CAPLUS (1907 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 156-34-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN Benzeneethanamine, α-methyl-, (αR)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzeneethanamine, α-methyl-, (R)-
CN Phenethylamine, α-methyl-, (-)- (8CI)
OTHER NAMES:
CN **(-)-(R)-Amphetamine**
CN **(-)-Amphetamine**
CN (-)-Phenaminum
CN (-)-Phenylisopropylamine
CN **(2R)-(-)-Amphetamine**
CN **(R)-(-)-Amphetamine**
CN **(R)-(-)-Amphetamine**
CN (R)-α-Methylphenethylamine
CN (R)-1-Methyl-2-phenylethylamine
CN (R)-1-Phenyl-2-aminopropane
CN (R)-1-Phenyl-2-propylamine
CN **(R)-Amphetamine**
CN **(R)-Amphetamine**
CN **L-(-)-Amphetamine**
CN **l-(-)-Amphetamine**
CN l-α-Methylphenethylamine
CN **L-Amphetamine**
CN **l-Amphetamine**
CN Levamfetamine
CN **Levoamphetamine**
FS STEREOSEARCH
MF C9 H13 N
CI COM
LC STN Files: ADISNEWS, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, GMELIN*, IFICDB, IFIPAT, IFIUDB, IPA, MRCK*, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, USPATOLD
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

738 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
742 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=>

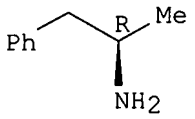
AB Selegiline (L-deprenyl) is a selective irreversible monoamine oxidase B inhibitor shown to be effective in the treatment of Parkinson's and **Alzheimer**'s diseases. Recent evidence suggests that selegiline may also be useful in treating specific aspects of cocaine and nicotine dependence, generating interest in this compound for the treatment of methamphetamine addiction. To investigate this, we performed a randomized, single-blind, placebo-controlled study to evaluate the safety of selegiline treatment (as compared to placebo), concurrent with i.v. methamphetamine (15 or 30 mg). Secondary study objectives included detns. of plasma levels of selegiline and its metabolites, evaluating whether selegiline administration altered the pharmacokinetics of methamphetamine or its metabolites, and evaluating whether selegiline treatment alters the subjective responses to methamphetamine. Twenty-four methamphetamine-dependent participants were randomized to treatment, and 9 of these (N = 5 selegiline, N = 4 placebo) completed the entire protocol. The principal finding from this study was that i.v. administration of moderate doses of methamphetamine was safely tolerated during treatment with selegiline. No participants had ECG changes, and there were no meaningful differences in any laboratory values either between groups at screening or as a result of the study procedures. In general, adverse events were mild or moderate, and no subjects were discontinued due to adverse events or serious adverse events. Selegiline treatment did not enhance any of the cardiovascular changes (heart rate, blood pressure) produced by methamphetamine administration. Selegiline treatment slightly increased methamphetamine associated "bad effects" but did not alter any other subjective effects. The elimination half-life of methamphetamine was .apprx.12 h, and selegiline did not alter clearance of methamphetamine. The available data suggest that selegiline is likely to be safe if used as a pharmacotherapy for methamphetamine dependence.

IT **156-34-3, L-Amphetamine**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(comprehensive assessment of safety of i.v. methamphetamine administration during treatment with selegiline)

RN 156-34-3 CAPLUS

CN Benzeneethanamine, α-methyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

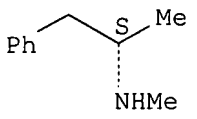
L8 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:238711 CAPLUS
DOCUMENT NUMBER: 142:291427
TITLE: Methods for treating **mild cognitive** impairment and **Alzheimer**'s disease
INVENTOR(S): Epstein, Mel H.; Wiig, Kjesten A.; Verheijen, Jeroen
PATENT ASSIGNEE(S): Sention, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 108 pp., Cont.-in-part of U.S. Ser. No. 444,970.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

L3 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2007 ACS on STN
RN 537-46-2 REGISTRY
ED Entered STN: 16 Nov 1984
CN Benzeneethanamine, N,α-dimethyl-, (αS)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzeneethanamine, N,α-dimethyl-, (S)-
CN Phenethylamine, N,α-dimethyl-, (S)-(+)- (8CI)
OTHER NAMES:
CN (+)-(S)-Deoxyephedrine
CN (+)-2-(N-Methylamino)-1-phenylpropane
CN **(+)-Methamphetamine**
CN (+)-Methylamphetamine
CN (+)-N,α-Dimethyl-β-phenylethylamine
CN (+)-N-Methylamphetamine
CN (S)-(+)-Deoxyephedrine
CN **(S)-(+)-Methamphetamine**
CN **(S)-Methamphetamine**
CN (S)-Methylamphetamine
CN **2S-(+)-Methamphetamine**
CN Corvitin
CN **d-(S)-Methamphetamine**
CN d-Deoxyephedrine
CN d-Desoxyephedrine
CN **d-Methamphetamine**
CN d-Methylamphetamine
CN d-N,α-Dimethylphenethylamine
CN d-N-Methylamphetamine
CN d-Phenylisopropylmethylamine
CN **L-Methamphetamine**
CN **Metamfetamine**
CN Metamphetamine
CN **Methamphetamine**
CN Methyl-β-phenylisopropylamine
CN Methylamphetamine
CN N-Methyl-1-phenyl-2-propanamine
CN N-Methylamphetamine
CN Norodin
CN NSC 25115
FS STEREOSEARCH
DR 139-47-9, 1690-86-4, 14611-50-8, 45952-89-4
MF C10 H15 N
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, PIRA, PROMT, PS, RTECS*, SCISEARCH, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, USPATOLD
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (+).



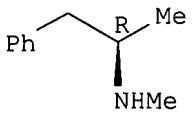
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4826 REFERENCES IN FILE CA (1907 TO DATE)

100 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4853 REFERENCES IN FILE CAPLUS (1907 TO DATE)
19 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L3 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2007 ACS on STN
RN 33817-09-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN Benzeneethanamine, N,α-dimethyl-, (αR)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzeneethanamine, N,α-dimethyl-, (R)-
CN Phenethylamine, N,α-dimethyl-, (-)- (8CI)
OTHER NAMES:
CN (-)-Deoxyephedrine
CN **(-)-Methamphetamine**
CN (-)-N-Methylamphetamine
CN (R)-(-)-Deoxyephedrine
CN **(R)-(-)-Methamphetamine**
CN (R)-Deoxyephedrine
CN **(R)-Methamphetamine**
CN (R)-Methylamphetamine
CN (R)-N-Methylamphetamine
CN **2R-(-)-Methamphetamine**
CN **D-Methamphetamine**
CN **l-(-)-Methamphetamine**
CN **l-Methamphetamine**
CN l-Methylamphetamine
CN **Levmetamfetamine**
CN NSC 6084
CN R(-)-N-Methylamphetamine
CN Vicks Inhaler
FS STEREOSEARCH
DR 13897-80-8, 45952-93-0
MF C10 H15 N
CI COM
LC STN Files: ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, DDFU, DRUGU, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, PROMT, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPATFULL, USPATOLD
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

364 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
367 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L8 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:493743 CAPLUS
DOCUMENT NUMBER: 144:481071
TITLE: Methods using amphetamine compounds for treating cognitive impairment in humans with multiple sclerosis
INVENTOR(S): Epstein, Mel H.; Wiig, Kjesten A.; Carpenter, Randall L.
PATENT ASSIGNEE(S): Sention, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 135 pp., Cont.-in-part of Appl. No. PCT/US04/015974.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006111448	A1	20060525	US 2005-133144	20050519
WO 2002039998	A2	20020523	WO 2001-US45793	20011031
WO 2002039998	A3	20040325		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002115725	A1	20020822	US 2001-3740	20011031
US 6828351	B2	20041207		
EP 1743631	A2	20070117	EP 2006-20373	20011031
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR, AL, LT, LV, MK, RO, SI				
US 2003119884	A1	20030626	US 2002-139606	20020502
US 2003232890	A1	20031218	US 2003-444970	20030523
US 2005059743	A1	20050317	US 2004-791223	20040302
WO 2005000203	A2	20050106	WO 2004-US15974	20040521
WO 2005000203	A3	20051229		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, US				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:		
US 2000-245323P	P	20001101
US 2001-3740	A2	20011031
WO 2001-US45793	A	20011031
US 2002-139606	A2	20020502
US 2003-444970	A2	20030523
US 2004-791223	A2	20040302
WO 2004-US15974	A2	20040521
EP 2001-987226	A3	20011031
US 2003-473168P	P	20030523

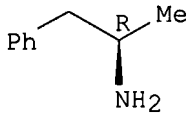
OTHER SOURCE(S): MARPAT 144:481071
AB Cognitive impairment in humans with multiple sclerosis are treated and

cognition is improved with an amphetamine compound In one embodiment, the method includes administering an **l-amphetamine** compound In another embodiment, the method includes administering an l-methamphetamine compound

IT **156-34-3**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amphetamine compds. for treatment of cognitive impairment in humans with multiple sclerosis)

RN 156-34-3 CAPLUS
CN Benzeneethanamine, α-methyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:382957 CAPLUS
DOCUMENT NUMBER: 144:419694
TITLE: Enteric coated compositions that release active ingredient(s) in gastric fluid and intestinal fluid
INVENTOR(S): Ayres, James W.
PATENT ASSIGNEE(S): State of Oregon Acting by and Through the State Board of Higher Education On Behalf of Oregon State University, USA
SOURCE: PCT Int. Appl., 184 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006044202	A2	20060427	WO 2005-US35787	20051003
WO 2006044202	A3	20070301		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1811975	A2	20070801	EP 2005-808429	20051003
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				

PRIORITY APPLN. INFO.: US 2004-620482P P 20041019
WO 2005-US35787 W 20051003

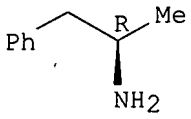
AB Embodiments of a pharmaceutical formulation comprising an enteric material are disclosed. The embodiments release at least a portion of an active ingredient upon contacting gastric fluid. The remaining portion of the formulation releases active ingredient upon contacting intestinal fluid. Certain embodiments of the pharmaceutical composition comprise at least one

active ingredient in a core and a leaky enteric coating, such as an enteric coating comprising a gastric fluid channeling agent. Other embodiments of the pharmaceutical composition comprise at least one active ingredient substantially homogeneously admixed with at least one enteric material, such as an enteric material comprising a gastric fluid channeling agent. Disclosed embodiments of the pharmaceutical composition may comprise a single active ingredient, or may comprise plural active ingredients. Generally, but not necessarily, the active ingredient has a window of absorption. The present disclosure also describes a method for treating a subject having a condition treatable by an active ingredient. The method comprises providing one or more embodiments of the pharmaceutical composition disclosed herein comprising an active ingredient suitable for treating the condition. The pharmaceutical composition is administered to the subject. A method for making embodiments of the disclosed composition also is described. The method comprises providing a core comprising an active ingredient. An enteric material is applied to at least a portion of the core, and generally on or about a substantial portion of the core, to form a coat. The composition is then made leaky. For example, hydrochlorothiazide (HCTZ) leaky enteric-coated beads were prepared by spray-layering drug on nonpareil sugar beads and then applying an enteric coating formulated to allow drug to be released in gastric fluid at programmed rates. Hydroxypropylyl Me cellulose (HPMC) was used which allowed drug leakage into gastric fluid and then provided rapid release of remaining drug from the formulation when exposed to intestinal fluid. A leaky enteric-coated bead formulation comprised, e.g., 7.5% of an enteric-coating polymer (Eudragit L30D-55 with 20% HPMC). A HCTZ loading solution contained hydrochlorothiazide 5.0 g, PVP K-30 3.0 g, water 30.0 mL, and 95% ethanol 500.0 mL. A leaky enteric coating composition contained Eudragit L30D-55 58.8%, talc 29.4% and HPMC E5 11.8%.

IT **156-34-3**
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(leaky enteric-coated oral compns. releasing drugs in both gastric and intestinal fluids)

RN 156-34-3 CAPLUS
CN Benzeneethanamine, α-methyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2006:109786 CAPLUS
DOCUMENT NUMBER:	144:267142
TITLE:	A comprehensive assessment of the safety of intravenous methamphetamine administration during treatment with selegiline
AUTHOR(S):	Newton, Thomas F.; De La Garza, Richard; Fong, Tim; Chiang, Nora; Holmes, Tyson H.; Bloch, Daniel A.; Anderson, Ann; Elkashef, Ahmed
CORPORATE SOURCE:	David Geffen School of Medicine, Department of Psychiatry and Biobehavioral Sciences, The University of California at Los Angeles, Los Angeles, CA, USA
SOURCE:	Pharmacology, Biochemistry and Behavior (2005), 82(4), 704-711 CODEN: PBBHAU; ISSN: 0091-3057
PUBLISHER:	Elsevier B.V.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

US 2005059743	A1	20050317	US 2004-791223		20040302
WO 2002039998	A2	20020523	WO 2001-US45793		20011031
WO 2002039998	A3	20040325			

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002115725	A1	20020822	US 2001-3740	20011031
US 6828351	B2	20041207		
EP 1743631	A2	20070117	EP 2006-20373	20011031

R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR, AL, LT, LV, MK, RO, SI

US 2003119884	A1	20030626	US 2002-139606	20020502
US 2003232890	A1	20031218	US 2003-444970	20030523
AU 2004251596	A1	20050106	AU 2004-251596	20040521
CA 2567746	A1	20050106	CA 2004-2567746	20040521
WO 2005000203	A2	20050106	WO 2004-US15974	20040521
WO 2005000203	A3	20051229		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, US

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1635851	A2	20060322	EP 2004-752902	20040521

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

CN 1826105	A	20060830	CN 2004-80021116	20040521
JP 2007502863	T	20070215	JP 2006-533278	20040521
US 2006111448	A1	20060525	US 2005-133144	20050519
MX 2005PA12614	A	20060823	MX 2005-PA12614	20051122
US 2007117869	A1	20070524	US 2006-557095	20060303
US 2007099999	A1	20070503	US 2006-636644	20061208
US 2007100000	A1	20070503	US 2006-636702	20061208
US 2007197663	A1	20070823	US 2006-636703	20061208

PRIORITY APPLN. INFO.:

US 2000-245323P	P	20001101
US 2001-3740	A2	20011031
WO 2001-US45793	A	20011031
US 2002-139606	A2	20020502
US 2003-444970	A2	20030523
EP 2001-987226	A3	20011031
WO 2001-US145793	A	20011031
US 2003-473168P	P	20030523
US 2004-791223	A	20040302
WO 2004-US15974	W	20040521
US 2006-557095	A1	20060303

OTHER SOURCE(S): MARPAT 142:291427

AB **Mild cognitive** impairment and **Alzheimer**'s disease are treated with an amphetamine compound In one embodiment, the method includes administering an 1-amphetamine compound In another embodiment, the method includes administering an 1-methamphetamine compound

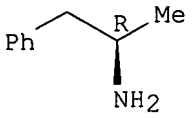
IT **156-34-3, L-Amphetamine**

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)
(amphetamine for treating **mild cognitive** impairment and **Alzheimer**'s disease)

RN 156-34-3 CAPLUS
CN Benzeneethanamine, α-methyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1124587 CAPLUS
DOCUMENT NUMBER: 142:69188
TITLE: Combination therapy for the treatment of diabetes
INVENTOR(S): Erondu, Ngozi E.; Fong, Tung M.; MacNeil, Douglas J.; Van Der Ploeg, Leonardus H. T.; Kanatani, Akio
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Banyu Pharmaceutical Co., Ltd.
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004110375	A2	20041223	WO 2004-US17291	20040602
WO 2004110375	A3	20050512		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1635832	A2	20060322	EP 2004-753999	20040602
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2007099884	A1	20070503	US 2005-559206	20051202
PRIORITY APPLN. INFO.:			US 2003-476388P	P 20030606
			WO 2004-US17291	W 20040602

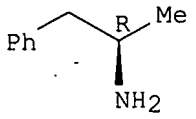
OTHER SOURCE(S): MARPAT 142:69188

AB The present invention relates to compns. comprising an anti-obesity agent and an anti-diabetic agent useful for the treatment of diabetes, diabetes associated with obesity and diabetes-related disorders. The present invention further relates to methods of treating or preventing obesity, and obesity-related disorders, in a subject in need thereof by administering a composition of the present invention. The present invention further provides for pharmaceutical compns., medicaments, and kits useful in carrying out these methods.

IT **156-34-3, Levamfetamine**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy of diabetes and diabetes-related disorders using antiobesity agent and antidiabetic agent and other agents)

RN 156-34-3 CAPLUS
CN Benzeneethanamine, α-methyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



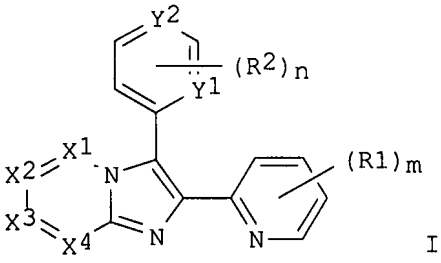
L8 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:989070 CAPLUS
DOCUMENT NUMBER: 142:85696
TITLE: Selegiline (l-deprenyl) as a unique neuroprotective agent for chronic neurodegenerative disorders- a lesson from MAO inhibition
AUTHOR(S): Wu, Ruey-Meei; Murphy, Dennis L.; Chiueh, Chuang C.
CORPORATE SOURCE: Department of Neurology, National Taiwan University Hospital, College of Medicine, National Taiwan University, Taipei, 100, Taiwan
SOURCE: Current Medicinal Chemistry: Central Nervous System Agents (2004), 4(4), 255-267
CODEN: CMCCCO; ISSN: 1568-0150
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The purpose of this review is to describe recent advances in understanding the neuroprotective effects of selegiline (N-propanyl-**l-amphetamine**; l-deprenyl) and the development of a variety of novel and interesting propargyl compds. that might be potentially useful in the treatment of chronic neurodegenerative brain disorders. Selegiline is a selective, noncompetitive, irreversible inhibitor of monoamine oxidase (MAO) B, and is widely used as an adjunct to L-DOPA in the treatment of Parkinson's disease. Recent interest in selegiline has focused on its complex neuroprotective actions against a variety of neurotoxins, and on the pathol. processes of oxidative stress and apoptosis which cause neuronal death in chronic neurodegenerative brain disorders, such as Parkinson's disease, **Alzheimer**'s disease, and amyotrophic lateral sclerosis. These neuroprotective effects of selegiline are due not only to MAO-B inhibition, but also to many other effects, such as suppression of free radical formation elicited by MPP+ and glutamate, up-regulation of the antioxidative enzymes, superoxide dismutase and catalase, induction of proteins interfering with the apoptotic pathway, and expression of neurotrophic factors. Recent mol. biol. evidence suggests that selegiline may also alter the expression of glyceraldehyde-3-phosphate dehydrogenase (GAPDH) and other redox active mols. such as thioredoxin in brain neurons. These unique neuroprotective mechanisms of selegiline may provide models for the synthesis of new N-propargyl analogs with different structure-activity relationships, and for the development of therapeutic strategies designed to prevent the evolution of pathol. neurodegeneration.
REFERENCE COUNT: 167 THERE ARE 167 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:220155 CAPLUS
DOCUMENT NUMBER: 140:270866
TITLE: Preparation of (pyridinyl)(pyrimidinyl)imidazo[1,2-a]pyridines as TGFβ receptor type I antagonists for treatment of fibrotic disorders and tumors
INVENTOR(S): Lee, Wen-cherng; Carter, Mary Beth; Sun, Lihong;

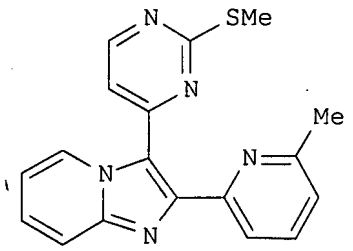
Chuaqui, Claudio; Singh, Juswinder; Boriack-Sjodin, Paula; Choi, Michael S.
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004021989	A2	20040318	WO 2003-US27721	20030905
WO 2004021989	A3	20040923		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2497968	A1	20040318	CA 2003-2497968	20030905
AU 2003270318	A1	20040329	AU 2003-270318	20030905
EP 1546112	A2	20050629	EP 2003-752004	20030905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003014052	A	20050705	BR 2003-14052	20030905
CN 1694871	A	20051109	CN 2003-824866	20030905
JP 2006502164	T	20060119	JP 2004-534570	20030905
NZ 539068	A	20061027	NZ 2003-539068	20030905
MX 2005PA02442	A	20050930	MX 2005-PA2442	20050303
ZA 2005001863	A	20051130	ZA 2005-1853	20050303
NO 2005001493	A	20050321	NO 2005-1493	20050321
US 2006135517	A1	20060622	US 2005-526653	20051101
PRIORITY APPLN. INFO.:			US 2002-408812P P	20020906
			WO 2003-US27721 W	20030905

OTHER SOURCE(S): MARPAT 140:270866
GI



I



II

AB Title compds. I [wherein X1, X2, X3, X4 = independently CRx or N, only two of them can be N simultaneously; Y1, Y2 = independently CRa or N, at least one of them must be N; R1 = independently alkyl, alkenyl, alkynyl, alkoxy, acyl, urea, cycloalkylsulfanyl, etc.; R2 = independently alkyl, alkenyl, alkynyl, acyl, halo, -N(alkyl)(cycloalkyl), heteroaroyl, etc.; m = 0-4; n = 0-3; Rx, Ra = independently hydrogen, alkyl, alkenyl, hydroxy, guanidino, amidino, cycloalkylcarbonylamino, etc.; and pharmaceutically acceptable salts or N-oxides thereof] were prepared as antagonists against transforming growth factor β (TGFβ) family type I receptors,

Alk5 and Alk4. For example, methylation of 2-mercapto-4-methylpyrimidine with MeI, followed by reaction with 6-methylpyridine-2-carboxylic acid Et ester and cyclocondensation with 2-aminopyridine, gave II. I exhibited TGFβ-induced PAI-Luciferase reporter activity with IC50 values of less than 10μM and cytotoxicity with LD25 values greater than 10μM. Thus, I and their pharmaceutical compns. are useful as antagonists for preventing and/or treating numerous diseases, including fibrotic disorders and tumors.

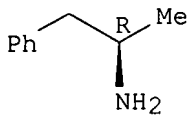
IT **156-34-3**

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (pyridinyl)(pyrimidinyl)imidazo[1,2-a]pyridines as TGFβ receptor type I antagonists for treatment of fibrotic disorders and tumors)

RN 156-34-3 CAPLUS

CN Benzeneethanamine, α-methyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:434536 CAPLUS

DOCUMENT NUMBER: 139:22115

TITLE: Preparation of 4-aminoquinolines as melanin concentrating hormone receptor antagonists, particularly MCH-1R antagonists.

INVENTOR(S): Devita, Robert J.; Chang, Lehua; Hoang, Myle Thi; Jiang, Jinlong; Lin, Peter; Sailer, Andreas W.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

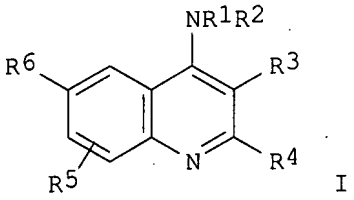
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003045920	A1	20030605	WO 2002-US37510	20021122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2468159	A1	20030605	CA 2002-2468159	20021122
AU 2002352868	A1	20030610	AU 2002-352868	20021122
EP 1451156	A1	20040901	EP 2002-789827	20021122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005518365	T	20050623	JP 2003-547372	20021122
US 2005009815	A1	20050113	US 2004-496614	20040525

PRIORITY APPLN. INFO.: US 2001-333464P P 20011127
WO 2002-US37510 W 20021122

OTHER SOURCE(S): MARPAT 139:22115

GI



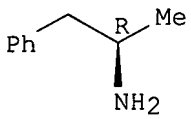
AB Title compds. [I; R1 R2 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl; R1R2N = (substituted) heterocyclyl; R3, R4 = H, halo, (substituted) alkyl, perfluoroalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloheteroalkyl, cycloheteroalkylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, OR7, NR7R7, CO2R7, cyano, CONR7R7; R3R4 = atoms to form a (substituted) 5-7 membered (hetero)cycloalkyl; R5 = H, halo, alkyl, perfluoroalkyl, OR7, NR7R7; R6 = (CH2)nR7, (CH2)naryl-R7, (CH2)n-heteroaryl-R7, (CH2)n-heterocycloalkyl-R7, (CH2)nCN, (CH2)nCON(R7)2, (CH2)nCO2R7, (CH2)nCOR7, (CH2)nNR7COR7, (CH2)nNR7CO(CH2)nSR7 (CH2)nNR7CO2R7, (CH2)nNR7CON(R7)2, (CH2)nNR7SO2R7, (CH2)nSOpR7, (CH2)nSO2N(R7)2, (CH2)nOR7, (CH2)nOC(O)R7, (CH2)nOCO2R7, (CH2)nO2CN(R7)2, (CH2)nN(R7)2, (CH2)nNR7SO2N(R7)2; R7 = H, (substituted) alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, aralkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkenyl, heteroarylalkenyl, cycloalkylalkenyl, heterocycloalkylalkenyl; n = 0-5; p = 0-2], were prepared Thus, 2-propylquinoline-4,6-diamine and (2E)-3-(4-chlorophenyl)prop-2-enoyl chloride were stirred 6 h in HOAc to give (2E)-N-(4-amino-2-propylquinolin-6-yl)-3-(4-chlorophenyl)prop-2-enamide. I are useful for the treatment or prevention of obesity or eating disorders, osteoarthritis, certain cancers, AIDS wasting, cachexia, frailty, mental disorders, stress, cognitive disorders, sexual function, reproductive function, kidney function, locomotor disorders, attention deficit disorder, substance abuse disorders, dyskinesias, Huntington's disease, epilepsy, memory function, and spinal muscular atrophy. I showed IC50 = 0.1-10000 nM for MCH-1R receptor binding activity.

IT **156-34-3, Levamfetamine**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 4-aminoquinolines as melanin concentrating hormone receptor antagonists, particularly MCH-1R antagonists)

RN 156-34-3 CAPLUS

CN Benzeneethanamine, α-methyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

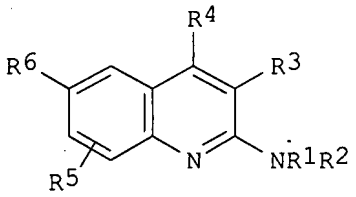
L8 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:434303 CAPLUS
DOCUMENT NUMBER: 139:36445
TITLE: Preparation of 2-aminoquinolines as melanin concentrating hormone receptor (MCH-1R) antagonists.
INVENTOR(S): Devita, Robert J.; Chang, Lehua; Chaung, Danny; Hoang, Myle; Jiang, Jinlong; Lin, Peter; Sailer, Andreas W.;

	Young, Jonathan R.
PATENT ASSIGNEE(S):	Merck & Co., Inc., USA
SOURCE:	PCT Int. Appl., 178 pp.
	CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003045313	A2	20030605	WO 2002-US37556	20021122
WO 2003045313	A3	20030904		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2468015	A1	20030605	CA 2002-2468015	20021122
AU 2002352878	A1	20030610	AU 2002-352878	20021122
EP 1450801	A2	20040901	EP 2002-789837	20021122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005519876	T	20050707	JP 2003-546818	20021122
US 2005026915	A1	20050203	US 2004-496615	20040525
US 7084156	B2	20060801		

PRIORITY APPLN. INFO.:	US 2001-333581P	P	20011127
	WO 2002-US37556	W	20021122
OTHER SOURCE(S):	MARPAT 139:36445		

GI



I

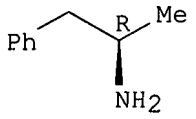
AB Title compds. [I; R1, R2 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkylalkyl, aralkyl, etc.; R1R2N = 4-11 membered (bridged) (substituted) heterocyclyl; R3, R4 = H, halo, (substituted) alkyl, alkenyl, alkynyl, perfluoroalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaralkyl, OR7, N(R7)2, cyano, etc.; R3R4 = atoms to form 5-7 membered (substituted) ring; R5 = H, halo, alkyl, perfluoroalkyl, OR7, N(R7)2; R6 = (CH2)nR7, (CH2)nCN, (CH2)nCO2R7, (CH2)nOR7, (CH2)nN(R7)2, etc.; R7 = H, alkyl, aryl, heteroaryl, cycloalkyl, aralkyl, aralkenyl, cycloalkylalkenyl, etc.; n = 0-5], were prepared for the treatment or prevention of obesity, eating disorders, osteoarthritis, cancer, AIDS wasting, cachexia, frailty, mental disorders, stress, cognitive disorders, sexual function, reproductive function, kidney function, locomotor disorders, attention deficit disorder (ADD), substance abuse disorders and dyskinesias, Huntington's disease, epilepsy, memory function, and spinal muscular atrophy. Thus, 2-piperidin-1-ylquinolin-6-amine and

(2E)-3-(4-chlorophenyl)prop-2-enoyl chloride were stirred 3 h in HOAc to give (2E)-3-(4-chlorophenyl)-N-(2-piperidin-1-ylquinolin-6-yl)prop-2-enamide hydrochloride. I bound to MCH-1R receptors with IC50 = 0.1-10000 nM.

IT **156-34-3, Levamfetamine**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of 2-aminoquinolines as melanin concentrating hormone receptor (MCH-1R) antagonists)

RN 156-34-3 CAPLUS
CN Benzeneethanamine, α-methyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:964140 CAPLUS
DOCUMENT NUMBER: 138:33353
TITLE: Preparation and locomotor activity of (R,R'), (R,S')-amphetaminil
INVENTOR(S): Lederman, Seth; Leventer, Steve; Kucharik, Robert, Jr.
PATENT ASSIGNEE(S): Vela Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002100346	A2	20021219	WO 2002-US18665	20020611
WO 2002100346	A3	20030403		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003118646	A1	20030626	US 2001-992235	20011106
AU 2002312478	A1	20021223	AU 2002-312478	20020611

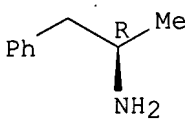
PRIORITY APPLN. INFO.:		
US 2001-297386P	P	20010611
US 2001-992235	A	20011106
WO 2002-US18665	W	20020611

AB (R,R'),(R,S') forms of amphetaminil substantially free of (S,S'),(S,R')-amphetaminil are prepared and their locomotor activity are disclosed. Thus, (R,R'),(R,S')-amphetaminil sulfate (I) were prepared by the reaction of (1S,2R)-(+)-norephedrine-HCl with PCl5 followed by the hydrogenation of the resulting norchloroephedrine-HCl, and finally reaction of the (-)-amphetamine obtained with benzaldehyde in the presence of NaCN in 10% H2SO4. I increased locomotor activity only at the highest dose of 10 mg/kg.

IT **156-34-3P**, (-)-Amphetamine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(in amphetaminil isomers preparation; preparation and locomotor activity of (R,R'),(R,S')-amphetaminil)
RN 156-34-3 CAPLUS
CN Benzeneethanamine, α-methyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

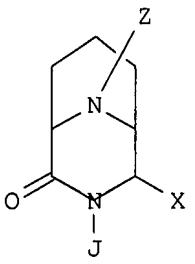


L8 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:868740 CAPLUS
DOCUMENT NUMBER: 137:370075
TITLE: Preparation of diazabicyclo[3.3.1]nonane derivatives as FKBP-ligands
INVENTOR(S): Guo, Chuangxing; Augelli-Szafran, Corinne E.; Barta, Nancy Sue; Bender, Steven Lee; Bigge, Christopher Franklin; Caprathe, Bradley William; Chatterjee, Arindam; Deal, Judith; Dong, Liming; Fay, Lorraine Kathleen; Hou, Xinjun; Hudack, Raymond Andrew, Jr.
PATENT ASSIGNEE(S): Agouron Pharmaceuticals, Inc., USA; Warner-Lambert Company
SOURCE: PCT Int. Appl., 177 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

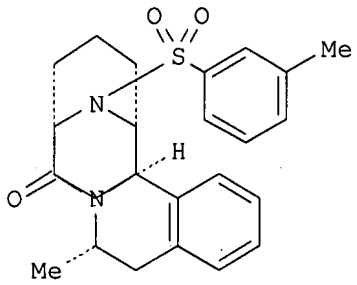
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002089806	A1	20021114	WO 2002-US14966	20020510
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2446795	A1	20021114	CA 2002-2446795	20020510
AU 2002303713	A1	20021118	AU 2002-303713	20020510
EP 1423119	A1	20040602	EP 2002-731761	20020510
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002010060	A	20040817	BR 2002-10060	20020510
JP 2004532854	T	20041028	JP 2002-586941	20020510
MX 2003PA10255	A	20050307	MX 2003-PA10255	20031110

PRIORITY APPLN. INFO.:	US 2001-289828P	P	20010510
	WO 2002-US14966	W	20020510

OTHER SOURCE(S): MARPAT 137:370075
GI



I



II

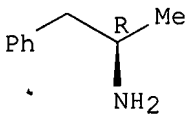
AB Title compds. I [Z = sulfonyl, acyl, etc.; J = H, alk(en)yl, cycloalkyl, aryl, heteroaryl; X = H, CN, alkoxy, dimethoxymethyl, oxygen (when the C-X bond is a double bond); X, J taken together with the N to form a (un)substituted heteroaryl, heterocycloalkyl] were prepared Over 130 example compds. were prepared and tested. For instance, 2,6-pyrdinedicarboxylic acid was reduced to the corresponding cis-piperidine dicarboxylic acid (H2O, NaOH, H2-Rh/Al, 55 psi, 48 h) and converted to the N-Cbz derivative This intermediate was converted to the bicyclic anhydride (Ac2O, 70°) and subsequently reacted with **L-amphetamine** to provide the corresponding imide (Ac2O, 110°). Reduction of the imide (THF/MeOH, NaBH4, -5°, 55 min), cyclization (CH2Cl2, TFA), removal of the Cbz group (EtOH/EtOAc, H2-Pd/C) and sulfonylation with m-toluenesulfonyl chloride provided II. Compds. of the invention inhibit FKBP-12 rotamase (peptidyl-prolyl isomerase) activity; II had Ki = 0.32 μM. I are useful for the treatment of peripheral neuropathies.

IT **156-34-3, L-Amphetamine**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of diazabicyclo[3.3.1]nonane derivs. as inhibitors of rotamase)

RN 156-34-3 CAPLUS

CN Benzeneethanamine, α-methyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:521416 CAPLUS

DOCUMENT NUMBER: 137:57581

TITLE: Use of catecholamine reuptake inhibitors to enhance memory

INVENTOR(S): Epstein, Mel H.; Wiig, Kjesten A.

PATENT ASSIGNEE(S): Sention, Inc., USA

SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053104	A2	20020711	WO 2002-US34	20020102
WO 2002053104	A3	20030410		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002243451	A1	20020716	AU 2002-243451		20020102
US 2002161002	A1	20021031	US 2002-39229		20020102
PRIORITY APPLN. INFO.:			US 2001-259374P	P	20010102
			WO 2002-US34	W	20020102

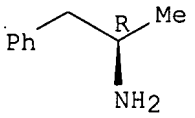
AB The invention provides methods and reagents for enhancing memory, e.g., to increase memory function such as long-term memory and recall ability. The methodol. of the invention uses catecholamine reuptake inhibitors.

IT **156-34-3**, R-(-)-Amphetamine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(catecholamine reuptake inhibitors to enhance memory)

RN 156-34-3 CAPLUS

CN Benzeneethanamine, α-methyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:136040 CAPLUS
DOCUMENT NUMBER: 136:189352
TITLE: Desmethylselegiline pharmaceuticals
INVENTOR(S): Blume, Cheryl D.; Disanto, Anthony R.
PATENT ASSIGNEE(S): Somerset Pharmaceuticals, Inc., USA
SOURCE: U.S., 34 pp., Cont.-in-part of Appl. No. PCT/US96/01561.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6348208	B1	20020219	US 1996-679330	19960712
WO 9622068	A2	19960725	WO 1996-US1561	19960111
WO 9622068	A3	19961114		

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CN 1178462	A	19980408	CN 1996-192486	19960111
AU 9892358	A	19990211	AU 1998-92358	19981112
AU 719447	B2	20000511		
US 6299901	B1	20011009	US 1999-262845	19990305
US 2001018457	A1	20010830	US 2001-805281	20010313

US 6562364	B2	20030513			
US 2001056126	A1	20011227	US 2001-895718		20010629
US 6419948	B2	20020716			
US 2002037930	A1	20020328	US 2001-940252		20010827
US 6528082	B2	20030304			
US 2002064552	A1	20020530	US 2001-960277		20010921
US 6562365	B2	20030513			
US 2003194432	A1	20031016	US 2001-26159		20011221
US 6699495	B2	20040302			
US 2003195260	A1	20031016	US 2003-353324		20030128
US 2003191191	A1	20031009	US 2003-382126		20030304
US 2004228907	A1	20041118	US 2004-790658		20040301
US 2006167110	A1	20060727	US 2005-290772		20051130
PRIORITY APPLN. INFO.:			US 1995-372139	B2	19950113
			US 1995-1979P	P	19950731
			WO 1996-US1561	A2	19960111
			AU 1996-48644	A3	19960111
			US 1996-679328	A2	19960712
			US 1996-679330	A2	19960712
			US 1999-262845	A1	19990305
			US 1999-448483	A3	19991124
			US 2000-228431P	P	20000828
			US 2001-800022	A1	20010305
			US 2001-800040	A2	20010305
			US 2001-940252	A1	20010827
			US 2001-26159	A3	20011221
			US 2002-361609P	P	20020304
			US 2002-251727	A1	20020920
			US 2004-790658	A2	20040301
			US 2004-885221	A2	20040706

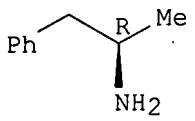
AB In particular, the present invention provides novel compns. and methods for using desmethylselegiline for selegiline-responsive diseases and conditions. Diseases and conditions responsive to selegiline include those produced by neuronal degeneration or neuronal trauma and those due to immune system dysfunction. Desmethylselegiline is the R-(-) enantiomer of N-methyl-N-(prop-2-ynyl)-2-aminophenylpropane. Claimed compns. include both the R-(-) isomer and mixts. of the R-(-) and S(+) isomers. Pharmaceutically acceptable acid addition salts may also be used. Effective dosages are a daily dose of at least about 0.015 mg/kg of body weight

IT **156-34-3, Levoamphetamine**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**levoamphetamine**; desmethylselegiline pharmaceuticals)

RN 156-34-3 CAPLUS

CN Benzeneethanamine, α-methyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:155178 CAPLUS
DOCUMENT NUMBER: 132:199060
TITLE: S-(+)-desmethylselegiline for pharmaceutical compositions.
INVENTOR(S): Disanto, Anthony R.
PATENT ASSIGNEE(S): Somerset Pharmaceuticals, Inc., USA
SOURCE: U.S., 34 pp., Cont.-in-part of U.S. Ser. No. 372,139.

CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6033682	A	20000307	US 1996-679328	19960712
WO 9622068	A2	19960725	WO 1996-US1561	19960111
WO 9622068	A3	19961114		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CN 1178462	A	19980408	CN 1996-192486	19960111
AU 9892358	A	19990211	AU 1998-92358	19981112
AU 719447	B2	20000511		
US 6319954	B1	20011120	US 1999-315840	19990521
US 6210706	B1	20010403	US 1999-448483	19991124
US 2001041747	A1	20011115	US 2001-800022	20010305
US 6455060	B2	20020924		
US 2001044473	A1	20011122	US 2001-800040	20010305
US 6375979	B2	20020423		
US 2001053798	A1	20011220	US 2001-885365	20010620
US 6420433	B2	20020716		
US 2002037930	A1	20020328	US 2001-940252	20010827
US 6528082	B2	20030304		
US 2003153624	A1	20030814	US 2002-251727	20020920
US 6759053	B2	20040706		
US 2003195260	A1	20031016	US 2003-353324	20030128
US 2003191191	A1	20031009	US 2003-382126	20030304
US 2004241220	A1	20041202	US 2004-885221	20040706
US 7144584	B2	20061205		
US 2006167110	A1	20060727	US 2005-290772	20051130

PRIORITY APPLN. INFO.:

US 1995-372139	A2	19950113
US 1995-1979P	P	19950731
WO 1996-US1561	A2	19960111
AU 1996-48644	A3	19960111
US 1996-679328	A2	19960712
US 1996-679330	B2	19960712
US 1999-315840	A1	19990521
US 1999-448483	A3	19991124
US 2000-228431P	P	20000828
US 2001-800022	A1	20010305
US 2001-800040	A2	20010305
US 2001-940252	A1	20010827
US 2001-26159	A1	20011221
US 2002-361609P	P	20020304
US 2002-251727	A1	20020920
US 2004-790658	A2	20040301
US 2004-885221	A2	20040706

AB The present invention provides novel compns. and methods for using the S-(+) enantiomer of desmethylselegiline [(N-methyl-N-(prop-2-ynyl)-2-aminophenylpropane)] (I) , for the treatment of selegiline-responsive diseases and conditions. Diseases and conditions responsive to selegiline include those produced by neuronal degeneration or neuronal trauma and those due to immune system dysfunction. Effective dosages are a daily dose of at least about 0.015 mg/kg of body weight Thus, tablets and capsules containing I are prepared from I 1-5, microcryst. cellulose 86, lactose 41.6, citric acid 0.5-2, citric acid 0.5-2, and magnesium stearate 0.4 mg/unit

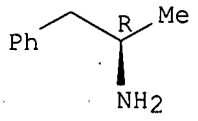
dose with an approx. 1:1 ratio of citric acid and sodium citrate. Both the R(-)- and S(+)-enantiomers significantly enhanced [3H]-dopamine uptake and the survival of TH pos. cells. In this model, the relative potency of both enantiomers appears to be equal to treatment with 50 μM selegiline.

IT **156-34-3, L-Amphetamine**
RL: RCT (Reactant); RACT (Reactant or reagent)
(S-(+)-desmethylselegiline for pharmaceutical compns.)

RN 156-34-3 CAPLUS

CN Benzeneethanamine, α-methyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 18 MEDLINE on STN

ACCESSION NUMBER: 90143749 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2515726
TITLE: Pharmacokinetics and metabolism of selegiline.
AUTHOR: Heinonen E H; Myllyla V; Sotaniemi K; Lamintausta R; Salonen J S; Anttila M; Savijarvi M; Kotila M; Rinne U K
CORPORATE SOURCE: Farmos Group Ltd, Research Center, Turku, Finland.
SOURCE: Acta neurologica Scandinavica. Supplementum, (1989) Vol. 126, pp. 93-9.
Journal code: 0370337. ISSN: 0065-1427.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199003
ENTRY DATE: Entered STN: 28 Mar 1990
Last Updated on STN: 6 Feb 1998
Entered Medline: 5 Mar 1990

AB Selegiline is readily absorbed from the gastrointestinal tract. It is distributed rapidly into the tissues, including the brain. It is the L-form of selegiline that is an active MAO-B inhibitor, the D-(+)-form being 25 times less active. Selegiline is metabolised into L-(-)-desmethylselegiline (DES), **L-(-)-amphetamine** (A) and L-(-)-methamphetamine (MA), mainly in the liver. We measured the steady state concentrations of the metabolites in the serum and cerebrospinal fluid (CSF) of patients with Parkinson's or **Alzheimer**'s diseases who were on continuous selegiline therapy. The mean concentrations in serum and CSF were similar, and were not affected by the addition of levodopa. The mean concentrations of patients with **Alzheimer**'s or Parkinson's disease were 6.5 +/- 2.5 ng/ml for A, 14.7 +/- 6.5 ng/ml for MA and 0.9 +/- 0.7 ng/ml for DES. The metabolites of selegiline were excreted in urine, and the recovery as metabolites was 87%. Due to the stereospecificity and the low CSF concentrations of the (-)amphetamine metabolites during the therapy with 10 mg selegiline, these metabolites do not seem to contribute significantly to the clinical efficacy of selegiline.

L8 ANSWER 16 OF 18 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1994:81973 BIOSIS
DOCUMENT NUMBER: PREV199497094973
TITLE: Chronic L-deprenyl or **L-amphetamine**:

Equal cognitive enhancement, unequal MAO inhibition.
AUTHOR(S): Gelowitz, Douglas L.; Richardson, J. Steven [Reprint author]; Wishart, Thomas B.; Yu, Peter H.; Lai, Chien-Tsai
CORPORATE SOURCE: Dep.Pharmacol. Psychiatry, Univ. Saskatchewan, Saskatoon, Saskatchewan S7N 0W0, Canada
SOURCE: Pharmacology Biochemistry and Behavior, (1994) Vol. 47, No. 1, pp. 41-45.
CODEN: PBBHAU. ISSN: 0091-3057.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Feb 1994
Last Updated on STN: 23 Feb 1994

AB The effect of chronic (4 month), subcutaneous injections of saline, L-deprenyl (0.25 mg/kg), or **L-amphetamine** (0.25 mg/kg) on the acquisition of a learned spatial habit in a modified Morris Water Maze was investigated in middle aged rats. Injections, given three times weekly starting at 6 months of age, were continued during behavioral testing, which occurred at 10 months of age. The cognitive performance of the middle aged rats was compared to that of 2-month-old control rats. Twenty-four hours after the last behavioral test, the rats were sacrificed and their brains were removed, dissected, and frozen in liquid nitrogen. The activities of MAO-A and MAO-B in the lateral cortex were determined. Results indicate that rats in the L-deprenyl group, the **L-amphetamine** group, and the young control group all learned the water maze task equally rapidly and significantly faster than rats in the saline group. MAO-A did not differ among the saline, amphetamine, and young control rats, but MAO-B was significantly higher in the middle aged saline and **L-amphetamine** rats than in the young controls. Both MAO-A and MAO-B activities were significantly lower in the L-deprenyl group than in the other three groups. This indicates that low-dose L-deprenyl can also inhibit MAO-A following chronic SC administration. Moreover, the improved cognitive performance produced by L-deprenyl may not be due to its ability to inhibit MAO-B, but rather to some other effect such as the activation of growth factors. It remains to be determined whether this mechanism is produced by, shared with, or independent from deprenyl's amphetamine metabolites.

L8 ANSWER 17 OF 18 EMBASE
ACCESSION NUMBER: 2004505331 EMBASE
TITLE: Selegiline (l-deprenyl) as a unique neuroprotective agent for chronic neurodegenerative disorders - A lesson from MAO inhibition.
AUTHOR: Wu R.-M.; Murphy D.L.; Chiueh C.C.
CORPORATE SOURCE: R.-M. Wu, Department of Neurology, National Taiwan University Hospital, No. 7, Chung-Shan South Road, Taipei 100, Taiwan, Province of China. rmwu@ha.mc.ntu.edu.tw
SOURCE: Current Medicinal Chemistry - Central Nervous System Agents, (Dec 2004) Vol. 4, No. 4, pp. 255-267.
Refs: 167
ISSN: 1568-0150 CODEN: CMCCCO
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 9 Dec 2004
Last Updated on STN: 9 Dec 2004

AB The purpose of this review is to describe recent advances in understanding the neuroprotective effects of selegiline (N-propanyl-**l-amphetamine**; l-deprenyl) and the development of a variety of novel and interesting propargyl compounds that might be potentially useful in

the treatment of chronic neurodegenerative brain disorders. Selegiline is a selective, non-competitive, irreversible inhibitor of monoamine oxidase (MAO) B, and is widely used as an adjunct to L-dopa in the treatment of Parkinson's disease. Recent interest in selegiline has focused on its complex neuroprotective actions against a variety of neurotoxins, and on the pathological processes of oxidative stress and apoptosis which cause neuronal death in chronic neurodegenerative brain disorders, such as Parkinson's disease, **Alzheimer**'s disease, and amyotrophic lateral sclerosis. These neuroprotective effects of selegiline are due not only to MAO-B inhibition, but also to many other effects, such as suppression of free radical formation elicited by MPP(+) and glutamate, up-regulation of the antioxidative enzymes, superoxide dismutase and catalase, induction of proteins interfering with the apoptotic pathway, and expression of neurotrophic factors. Recent molecular biological evidence suggests that selegiline may also alter the expression of glyceraldehyde-3-phosphate dehydrogenase (GAPDH) and other redox active molecules such as thioredoxin in brain neurons. These unique neuroprotective mechanisms of selegiline may provide models for the synthesis of new N- propargyl analogues with different structure-activity relationships, and for the development of therapeutic strategies designed to prevent the evolution of pathologic neurodegeneration.

L8 ANSWER 18 OF 18 EMBASE

ACCESSION NUMBER: 1994019743 EMBASE
TITLE: Chronic L-deprenyl or **L-amphetamine**: Equal cognitive enhancement, unequal MAO inhibition.
AUTHOR: Gelowitz D.L.; Richardson J.S.; Wishart T.B.; Yu P.H.; Lai C.-T.
CORPORATE SOURCE: J.S. Richardson, Department of Pharmacology, University of Saskatchewan, Saskatoon, Sask. S7N 0W0, Canada
SOURCE: Pharmacology Biochemistry and Behavior, (1994) Vol. 47, No. 1, pp. 41-45.
ISSN: 0091-3057 CODEN: PBBHAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jan 1994
Last Updated on STN: 30 Jan 1994

AB The effect of chronic (4 month), subcutaneous injections of saline, L-deprenyl (0.25 mg/kg), or **L-amphetamine** (0.25 mg/kg) on the acquisition of a learned spatial habit in a modified Morris Water Maze was investigated in middle aged rats. Injections, given three times weekly starting at 6 months of age, were continued during behavioral testing, which occurred at 10 months of age. The cognitive performance of the middle aged rats was compared to that of 2-month-old control rats. Twenty-four hours after the last behavioral test, the rats were sacrificed and their brains were removed, dissected, and frozen in liquid nitrogen. The activities of MAO-A and MAO-B in the lateral cortex were determined. Results indicate that rats in the L-deprenyl group, the **L-amphetamine** group, and the young control group all learned the water maze task equally rapidly and significantly faster than rats in the saline group. MAO-A did not differ among the saline, amphetamine, and young control rats, but MAO-B was significantly higher in the middle aged saline and **L-amphetamine** rats than in the young controls. Both MAO-A and MAO-B activities were significantly lower in the L-deprenyl group than in the other three groups. This indicates that low-dose L-deprenyl can also inhibit MAO-A following chronic SC

administration. Moreover, the improved cognitive performance produced by L-deprenyl may not be due to its ability to inhibit MAO-B, but rather to some other effect such as the activation of growth factors. It remains to be determined whether this mechanism is produced by, shared with, or independent from deprenyl's amphetamine metabolites.

=> d his

(FILE 'HOME' ENTERED AT 16:08:31 ON 08 NOV 2007)

FILE 'REGISTRY' ENTERED AT 16:08:51 ON 08 NOV 2007
L1 503 S AMPHETAMINE
L2 3 S AMPHETAMINE AND AMFETAMINE
L3 3 S METAMFETAMINE AND METHAMPHETAMINE
L4 1 S AMPHETAMINE AND LEVO

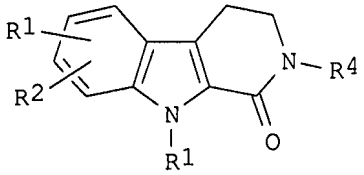
FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE' ENTERED AT 16:12:00 ON 08 NOV 2007
L5 338080 S ALZHEIMER OR DEMENTIA OR (SENILE (L) DEMENTIA) OR ALZHEIMER?
L6 346406 S L5 OR ((MILD (L) COGNITIVE) OR FORGETFULNESS)
L7 734 S L6 AND (300-62-9/RN OR AMPHETAMINE OR AMFETAMINE OR METHYLPH
L8 18 S L6 AND (156-34-3/RN OR LEVOAMPHETAMINE OR L-AMPHETAMINE OR L
L9 259 S L6 AND (METHAMPHETAMINE OR METHYLAMPHETAMINE OR DEOXYEPHEDRI
L10 13 S L6 AND (33817-09-3/RN OR LEVMETAMFETAMINE OR L-METHYLAMPHETA
L11 85 S L7 AND L9
L12 4 S L8 AND L10
L13 25 S L11 AND PD <=2001
L14 22 S L11 AND PD <=2000
L15 83146 S EPSTEIN OR WIIG OR VERHEIJEN
L16 0 S L15 AND L11
L17 10 S EPSTEIN/AU OR WIIG/AU OR VERHEIJEN/AU
L18 0 S L17 AND L11
L19 0 S L17 AND (L7 OR L9)
L20 0 S EPSTEIN/IV OR WIIG/IV OR VERHEIJEN/IV
L21 0 S EPSTEIN/AS OR WIIG/AS OR VERHEIJEN/AS
L22 0 S L17 AND ALZHEIMER?
L23 83 S L15 AND (ALZHEIMER?)
L24 0 S L23 AND (L7 OR L9)

=> d ibib abs 1-13 hit l10 hitstr

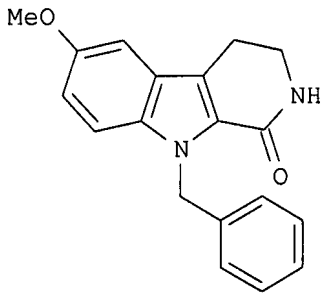
L10 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:254420 CAPLUS
DOCUMENT NUMBER: 146:401956
TITLE: New tetrahydro-β-carbolinone compounds having antiinflammatory activity: process for their preparation and pharmaceutical compositions containing them
INVENTOR(S): Rao, Yeleswarapu Koteswar; Baruah, Bipul; Rajagopalan, Ramanujam; Rao, Casturi Seshagiri
PATENT ASSIGNEE(S): Dr. Reddy's Research Foundation, India
SOURCE: Indian Pat. Appl., 49pp.
CODEN: INXXBQ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 2000MA01126	A	20050304	IN 2000-MA1126	20001226

PRIORITY APPLN. INFO.: IN 2000-MA1126 20001226
OTHER SOURCE(S): CASREACT 146:401956
GI



I



II

AB The invention relates to heterocyclic compds. of the general formula I, their derivates, their analogs, their tautomeric forms their stereoisomers their regioisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceuticals acceptable solvates and pharmaceutically acceptable compns. containing them. Compds. of formula I wherein R1 and R2 are independently H, halo, OH, CN, NO2, thio, (un)substituted amino, (un)substituted C1-6 alkyl, (un)substituted C2-6 alkenyl, etc.; R3 is (un)substituted C1-6 alkyl, (un)substituted C1-8 acyl, (un)substituted aryl, (un)substituted aralkyl, (un)substituted C2-6 alkenyl, etc.; R4 is H, (un)substituted C1-6 alkyl, (un)substituted C1-8 acyl, (un)substituted C2-6 alkenyl, (un)substituted (hetero)aryl, (un)substituted aralkyl, etc.; are claimed. Example compound II was prepared by cyclization of 4-methoxyaniline with 3-oxopiperidine-3-carboxylic acid Et ester to give 6-methoxy-2,3,4,9-tetrahydro-β-carbolin-1-one, which underwent alkylation with benzyl bromide to give compound II. All the invention compds. were evaluated for their antiinflammatory activity.

IT Analgesics
Anti-**Alzheimer**'s agents
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antibacterial agents
Antimigraine agents
Antipyretics
Antirheumatic agents
Antitumor agents
Antiulcer agents
Antiviral agents
Bronchodilators
Muscle relaxants
(preparation of tetrahydro-β-carbonlinones as antiinflammatory agents)

IT **Alzheimer**'s disease
Arthritis
Asthma
Atherosclerosis
Blood vessel, disease
Burn
Common cold
Dermatitis
Dermatitis
Dysmenorrhea
Eczema
Eye, disease
Fever and Hyperthermia
Gout
Headache
Hodgkin's disease
Inflammation
Influenza

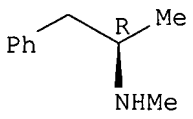
Myasthenia gravis
Myocardial ischemia
Neoplasm
Osteoarthritis
Pain
Psoriasis
Respiratory distress syndrome
Retinal disease
Retinitis
Rheumatoid arthritis
Sarcoidosis
Scleroderma
Uveitis
(treatment of; preparation of tetrahydro-β-carbonlinones as antiinflammatory agents)

IT 51-43-4, Epinephrine 58-08-2, Caffeine, biological studies 59-42-7, Phenylephrine 62-44-2, Phenacetin 76-57-3, Codeine 77-22-5, Caraminphen 77-23-6, Carbetapentane 90-82-4, Pseudoephedrine 101-40-6, Propylhexadrine 103-90-2, Acetaminophen 125-28-0, Hydrocodeine 125-71-3, Dextromethorphan 526-36-3, Xylometazoline 835-31-4, Nephazoline 1309-42-8, Magnesium hydroxide 1491-59-4, Oxymetazoline 8050-81-5, Simethicone 14838-15-4, Phenyl propanolamine 21645-51-2, Aluminum hydroxide, biological studies **33817-09-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of tetrahydro-β-carbonlinones as antiinflammatory agents)

IT **33817-09-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of tetrahydro-β-carbonlinones as antiinflammatory agents)

RN 33817-09-3 CAPLUS
CN Benzeneethanamine, N,α-dimethyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L10 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:493743 CAPLUS
DOCUMENT NUMBER: 144:481071
TITLE: Methods using amphetamine compounds for treating cognitive impairment in humans with multiple sclerosis
INVENTOR(S): Epstein, Mel H.; Wiig, Kjesten A.; Carpenter, Randall L.
PATENT ASSIGNEE(S): Sention, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 135 pp., Cont.-in-part of Appl. No. PCT/US04/015974.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006111448	A1	20060525	US 2005-133144	20050519
WO 2002039998	A2	20020523	WO 2001-US45793	20011031

WO 2002039998 A3 20040325
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002115725 A1 20020822 US 2001-3740 20011031
US 6828351 B2 20041207
EP 1743631 A2 20070117 EP 2006-20373 20011031
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR, AL, LT, LV, MK, RO, SI
US 2003119884 A1 20030626 US 2002-139606 20020502
US 2003232890 A1 20031218 US 2003-444970 20030523
US 2005059743 A1 20050317 US 2004-791223 20040302
WO 2005000203 A2 20050106 WO 2004-US15974 20040521
WO 2005000203 A3 20051229
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, US
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2000-245323P	P	20001101
US 2001-3740	A2	20011031
WO 2001-US45793	A	20011031
US 2002-139606	A2	20020502
US 2003-444970	A2	20030523
US 2004-791223	A2	20040302
WO 2004-US15974	A2	20040521
EP 2001-987226	A3	20011031
US 2003-473168P	P	20030523

OTHER SOURCE(S): MARPAT 144:481071

AB Cognitive impairment in humans with multiple sclerosis are treated and cognition is improved with an amphetamine compound In one embodiment, the method includes administering an l-amphetamine compound In another embodiment, the method includes administering an **l-methamphetamine** compound

AB Cognitive impairment in humans with multiple sclerosis are treated and cognition is improved with an amphetamine compound In one embodiment, the method includes administering an l-amphetamine compound In another embodiment, the method includes administering an **l-methamphetamine** compound

IT **Alzheimer**'s disease
Cognition enhancers
Cognitive disorders
Combination chemotherapy
Drug delivery systems
Human
Learning disorders
Multiple sclerosis
Pharmacokinetics
(amphetamine compds. for treatment of cognitive impairment in humans with multiple sclerosis)

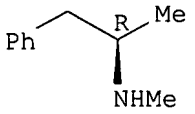
IT 300-62-9D, Amphetamine, compds. **33817-09-3**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amphetamine compds. for treatment of cognitive impairment in humans with multiple sclerosis)

IT **33817-09-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amphetamine compds. for treatment of cognitive impairment in humans with multiple sclerosis)

RN 33817-09-3 CAPLUS
CN Benzeneethanamine, N,α-dimethyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L10 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:109786 CAPLUS
DOCUMENT NUMBER: 144:267142
TITLE: A comprehensive assessment of the safety of intravenous methamphetamine administration during treatment with selegiline
AUTHOR(S): Newton, Thomas F.; De La Garza, Richard; Fong, Tim; Chiang, Nora; Holmes, Tyson H.; Bloch, Daniel A.; Anderson, Ann; Elkashef, Ahmed
CORPORATE SOURCE: David Geffen School of Medicine, Department of Psychiatry and Biobehavioral Sciences, The University of California at Los Angeles, Los Angeles, CA, USA
SOURCE: Pharmacology, Biochemistry and Behavior (2005), 82(4), 704-711
CODEN: PBBHAU; ISSN: 0091-3057
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Selegiline (L-deprenyl) is a selective irreversible monoamine oxidase B inhibitor shown to be effective in the treatment of Parkinson's and **Alzheimer**'s diseases. Recent evidence suggests that selegiline may also be useful in treating specific aspects of cocaine and nicotine dependence, generating interest in this compound for the treatment of methamphetamine addiction. To investigate this, we performed a randomized, single-blind, placebo-controlled study to evaluate the safety of selegiline treatment (as compared to placebo), concurrent with i.v. methamphetamine (15 or 30 mg). Secondary study objectives included detns. of plasma levels of selegiline and its metabolites, evaluating whether selegiline administration altered the pharmacokinetics of methamphetamine or its metabolites, and evaluating whether selegiline treatment alters the subjective responses to methamphetamine. Twenty-four methamphetamine-dependent participants were randomized to treatment, and 9 of these (N = 5 selegiline, N = 4 placebo) completed the entire protocol. The principal finding from this study was that i.v. administration of moderate doses of methamphetamine was safely tolerated during treatment with selegiline. No participants had ECG changes, and there were no meaningful differences in any laboratory values either between groups at screening or as a result of the study procedures. In general, adverse events were mild or moderate, and no subjects were discontinued due to adverse events or serious adverse events. Selegiline treatment did not enhance any of the cardiovascular changes (heart rate, blood pressure) produced by methamphetamine administration. Selegiline treatment slightly increased methamphetamine associated "bad effects" but did not alter any other subjective effects. The

elimination half-life of methamphetamine was .apprx.12 h, and selegiline did not alter clearance of methamphetamine. The available data suggest that selegiline is likely to be safe if used as a pharmacotherapy for methamphetamine dependence.

AB Selegiline (L-deprenyl) is a selective irreversible monoamine oxidase B inhibitor shown to be effective in the treatment of Parkinson's and **Alzheimer**'s diseases. Recent evidence suggests that selegiline may also be useful in treating specific aspects of cocaine and nicotine dependence, generating interest in this compound for the treatment of methamphetamine addiction. To investigate this, we performed a randomized, single-blind, placebo-controlled study to evaluate the safety of selegiline treatment (as compared to placebo), concurrent with i.v. methamphetamine (15 or 30 mg). Secondary study objectives included detns. of plasma levels of selegiline and its metabolites, evaluating whether selegiline administration altered the pharmacokinetics of methamphetamine or its metabolites, and evaluating whether selegiline treatment alters the subjective responses to methamphetamine. Twenty-four methamphetamine-dependent participants were randomized to treatment, and 9 of these (N = 5 selegiline, N = 4 placebo) completed the entire protocol. The principal finding from this study was that i.v. administration of moderate doses of methamphetamine was safely tolerated during treatment with selegiline. No participants had ECG changes, and there were no meaningful differences in any laboratory values either between groups at screening or as a result of the study procedures. In general, adverse events were mild or moderate, and no subjects were discontinued due to adverse events or serious adverse events. Selegiline treatment did not enhance any of the cardiovascular changes (heart rate, blood pressure) produced by methamphetamine administration. Selegiline treatment slightly increased methamphetamine associated "bad effects" but did not alter any other subjective effects. The elimination half-life of methamphetamine was .apprx.12 h, and selegiline did not alter clearance of methamphetamine. The available data suggest that selegiline is likely to be safe if used as a pharmacotherapy for methamphetamine dependence.

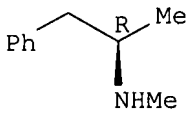
IT 51-64-9, D-Amphetamine 64-04-0, Phenethylamine 156-34-3, L-Amphetamine **33817-09-3**, D-Methamphetamine 56862-28-3, Desmethylselegiline
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(comprehensive assessment of safety of i.v. methamphetamine administration during treatment with selegiline)

IT **33817-09-3**, D-Methamphetamine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(comprehensive assessment of safety of i.v. methamphetamine administration during treatment with selegiline)

RN 33817-09-3 CAPLUS

CN Benzeneethanamine, N,α-dimethyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:955615 CAPLUS
DOCUMENT NUMBER: 143:415436
TITLE: Neuropharmacological, neuroprotective and amyloid precursor processing properties of selective MAO-B inhibitor antiparkinsonian drug, rasagiline
AUTHOR(S): Youdim, Moussa B. H.; Maruyama, Wakako; Naoi, Makato
CORPORATE SOURCE: Eve Topf and NPF Centers of Excellence for

Neurodegenerative Diseases Research and Department of Pharmacology, Technion-Rappaport Faculty of Medicine, Haifa, Israel
SOURCE: Drugs of Today (2005), 41(6), 369-391
CODEN: MDACAP; ISSN: 0025-7656
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Rasagiline (N-propargyl-1R-aminoindan) is a novel, highly potent, irreversible monoamine oxidase (MAO)-B inhibitor designed for use as an antiparkinsonian drug. Unlike selegiline, rasagiline is not derived from amphetamine or metabolized to neurotoxic **l-methamphetamine** derivative, and it does not have sympathomimetic activity. Moreover, at selective MAO-B inhibitory dosage, it does not induce a "cheese reaction.". Rasagiline is effective as monotherapy or as an adjunct to L-dopa for patients with early and late Parkinson's disease. Adverse events do not occur with greater frequency in subjects receiving rasagiline than in those on placebo. Its S-isomer, TVP1022, is more than a thousand times less potent as an MAO inhibitor. However, both drugs have neuroprotective activities in neuronal cell cultures in response to various neurotoxins, as well as in vivo (e.g., in response to global ischemia, neurotrauma, head injury, anoxia, etc.), indicating that MAO inhibition is not a prerequisite for neuroprotection. The neuroprotective activity of these drugs has been demonstrated to be associated with the propargylamine moiety, which protects mitochondrial viability and mitochondrial permeability transition pore by activating Bcl-2 and downregulating the Bax family of proteins. Rasagiline processes amyloid precursor protein (APP) into the neuroprotective-neurotropic soluble APPalpha (sAPPα) by protein kinase C- and mitogen-activated protein kinase-dependent activation of α-secretase, and increases nerve growth factor, glial cell-derived neurotropic factor (GDNF) and brain-derived neurotropic factor (BDNF) expression and proteins. Thus, rasagiline may induce neuroprotection, neuroplasticity and long-term potentiation. Rasagiline has therefore been chosen by the National Institutes of Health (NIH) to study its neuroprotective effects in neurodegenerative diseases. Long-term studies are required to evaluate the drug's disease-modifying prospects in Parkinson's and **Alzheimer**'s diseases.
AB A review. Rasagiline (N-propargyl-1R-aminoindan) is a novel, highly potent, irreversible monoamine oxidase (MAO)-B inhibitor designed for use as an antiparkinsonian drug. Unlike selegiline, rasagiline is not derived from amphetamine or metabolized to neurotoxic **l-methamphetamine** derivative, and it does not have sympathomimetic activity. Moreover, at selective MAO-B inhibitory dosage, it does not induce a "cheese reaction.". Rasagiline is effective as monotherapy or as an adjunct to L-dopa for patients with early and late Parkinson's disease. Adverse events do not occur with greater frequency in subjects receiving rasagiline than in those on placebo. Its S-isomer, TVP1022, is more than a thousand times less potent as an MAO inhibitor. However, both drugs have neuroprotective activities in neuronal cell cultures in response to various neurotoxins, as well as in vivo (e.g., in response to global ischemia, neurotrauma, head injury, anoxia, etc.), indicating that MAO inhibition is not a prerequisite for neuroprotection. The neuroprotective activity of these drugs has been demonstrated to be associated with the propargylamine moiety, which protects mitochondrial viability and mitochondrial permeability transition pore by activating Bcl-2 and downregulating the Bax family of proteins. Rasagiline processes amyloid precursor protein (APP) into the neuroprotective-neurotropic soluble APPalpha (sAPPα) by protein kinase C- and mitogen-activated protein kinase-dependent activation of α-secretase, and increases nerve growth factor, glial cell-derived neurotropic factor (GDNF) and brain-derived neurotropic factor (BDNF) expression and proteins. Thus, rasagiline may induce neuroprotection, neuroplasticity and long-term potentiation. Rasagiline has therefore been chosen by the National

Institutes of Health (NIH) to study its neuroprotective effects in neurodegenerative diseases. Long-term studies are required to evaluate the drug's disease-modifying prospects in Parkinson's and **Alzheimer**'s diseases.

IT Nervous system, disease
(degeneration; rasagiline is effective as monotherapy/adjunct to L-dopa in early and late Parkinson's disease patient with no greater adverse events, long-term study is needed to test disease-modifying prospects in Parkinson's and **Alzheimer**'s diseases)

IT Brain
Human
Parkinson's disease
(rasagiline is effective as monotherapy/adjunct to L-dopa in early and late Parkinson's disease patient with no greater adverse events, long-term study is needed to test disease-modifying prospects in Parkinson's and **Alzheimer**'s diseases)

IT 14611-51-9, Selegiline
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rasagiline is not derived from amphetamine or metabolized to neurotoxic **l-methamphetamine** derivative, does not have sympathomimetic activity, and at selective MAO-B inhibitory dosage, it does not induce "cheese reaction like selegiline)

REFERENCE COUNT: 159 THERE ARE 159 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:238711 CAPLUS
DOCUMENT NUMBER: 142:291427
TITLE: Methods for treating **mild cognitive** impairment and **Alzheimer**'s disease
INVENTOR(S): Epstein, Mel H.; Wiig, Kjesten A.; Verheijen, Jeroen
PATENT ASSIGNEE(S): Sention, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 108 pp., Cont.-in-part of U.S. Ser. No. 444,970.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005059743	A1	20050317	US 2004-791223	20040302
WO 2002039998	A2	20020523	WO 2001-US45793	20011031
WO 2002039998	A3	20040325		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002115725	A1	20020822	US 2001-3740	20011031
US 6828351	B2	20041207		
EP 1743631	A2	20070117	EP 2006-20373	20011031
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR, AL, LT, LV, MK, RO, SI				
US 2003119884	A1	20030626	US 2002-139606	20020502
US 2003232890	A1	20031218	US 2003-444970	20030523

disease)
IT Behavior
(locomotor; amphetamine for treating **mild cognitive** impairment and **Alzheimer**'s disease)
IT Memory, biological
(long-term; amphetamine for treating **mild cognitive** impairment and **Alzheimer**'s disease)
IT Behavior
(motor; amphetamine for treating **mild cognitive** impairment and **Alzheimer**'s disease)
IT Drug delivery systems
(oral; amphetamine for treating **mild cognitive** impairment and **Alzheimer**'s disease)
IT Behavior
(passive avoidance; amphetamine for treating **mild cognitive** impairment and **Alzheimer**'s disease)
IT Mental activity
(performance; amphetamine for treating **mild cognitive** impairment and **Alzheimer**'s disease)
IT Behavior
(recognition; amphetamine for treating **mild cognitive** impairment and **Alzheimer**'s disease)
IT Memory, biological
(short-term; amphetamine for treating **mild cognitive** impairment and **Alzheimer**'s disease)
IT Drug delivery systems
(sustained-release; amphetamine for treating **mild cognitive** impairment and **Alzheimer**'s disease)
IT 156-34-3, L-Amphetamine
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amphetamine for treating **mild cognitive** impairment and **Alzheimer**'s disease)
IT 51-64-9, D-Amphetamine 300-62-9, Amphetamine 537-46-2, **L-Methamphetamine**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amphetamine for treating **mild cognitive** impairment and **Alzheimer**'s disease)

L10 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:53466 CAPLUS
DOCUMENT NUMBER: 142:190096
TITLE: Rasagiline: Neurodegeneration, neuroprotection, and mitochondrial permeability transition
AUTHOR(S): Youdim, Moussa B. H.; Am, Orit Bar; Yogev-Falach, Merav; Weinreb, Orly; Maruyama, Wakako; Naoi, Makato; Amit, Tamar
CORPORATE SOURCE: Research and Department of Pharmacology, and Rappaport Family Research Institute, Technion-Faculty of Medicine, Eve Topf and USA National Parkinson Foundation Centers of Excellence for Neurodegenerative Diseases, Haifa, Israel
SOURCE: Journal of Neuroscience Research (2004), Volume Date 2005, 79(1 & 2), 172-179
CODEN: JNREDK; ISSN: 0360-4012
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Mitochondria are involved directly in cell survival and death. The assumption was made that drugs that protect mitochondrial viability and prevent apoptotic cascade-induced mitochondrial permeability transition pore (MPTp) opening will be cytoprotective. Rasagiline (N-propargyl-1R-aminoindan) is a novel, highly potent irreversible

disorders

INVENTOR(S): Dube, Daniel; Deschenes, Denis; Fortin, Rejean; Girard, Yves

PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.

SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

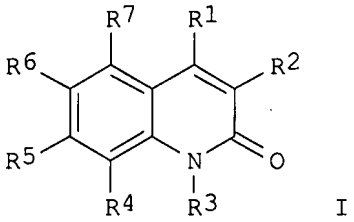
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003051878	A1	20030626	WO 2002-CA1914	20021211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2469048	A1	20030626	CA 2002-2469048	20021211
AU 2002350315	A1	20030630	AU 2002-350315	20021211
EP 1458718	A1	20040922	EP 2002-784961	20021211
EP 1458718	B1	20061025		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005520797	T	20050714	JP 2003-552762	20021211
AT 343577	T	20061115	AT 2002-784961	20021211
ES 2274111	T3	20070516	ES 2002-2784961	20021211
US 2005222194	A1	20051006	US 2004-498084	20040610

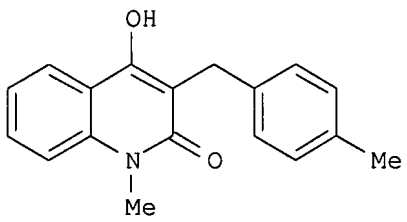
PRIORITY APPLN. INFO.: US 2001-340439P P 20011214
WO 2002-CA1914 W 20021211

OTHER SOURCE(S): MARPAT 139:69162

GI



I



II

AB Title compds. I [wherein R1 = H, halo, OH, N(R8)2, or (un)substituted alkyl, alkenyl, alkoxy, alkylthio, alkanoyl(oxy), alkoxycarbonyl, aryl, aralkyl, aryloxy, aralkoxy, arylthio, aroyl, or aroyloxy; R2 = (un)substituted benzyl, alkyl, alkenyl, or aroyl; R3 = (un)substituted alkyl, alkenyl, alkynyl, aryl, or aralkyl; R4-R7 = independently H, halo, or (un)substituted alkyl; or R3 and R4 may be joined together with the atoms to which they are attached to form a monocyclic ring; R8 = H or (un)substituted alkyl, alkenyl, or alkanoyl; and pharmaceutically acceptable salts, hydrates, esters, or tautomers thereof] were prepared as prostaglandin E receptor ligands (no data). For example, reaction of N-methyl-4-hydroxy-2-quinolone with 4-methylbenzaldehyde in the presence of Et3SiH and TFA in toluene gave II. I and pharmaceutical compns. comprising I may be useful for the treatment of pain, fever, inflammation,

and a broad variety of prostaglandin E mediated diseases and conditions (no data).

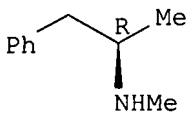
IT **Alzheimer**'s disease
Analgesics
Anti-**Alzheimer**'s agents
Anti-inflammatory agents
Antiasthmatics
Anticoagulants
Antipyretics
Antirheumatic agents
Antitumor agents
Antiulcer agents
Arthritis
Asthma
Autoimmune disease
Blood coagulation disorders
Burn
Drug delivery systems
Dysmenorrhea
Gastrointestinal agents
Glaucoma (disease)
Gout
Headache
Hemophilia
Human
Immune disease
Inflammation
Influenza
Kidney, disease
Myositis
Osteoarthritis
Osteoporosis
Rheumatic fever
Rheumatoid arthritis
Strain
Sunburn
Thrombosis
(preparation of quinolinone prostaglandin E receptor ligands for treatment of pain, fever, inflammation, and other prostanoid mediated diseases)

IT 50-78-2, Aspirin 51-43-4, Epinephrine 58-08-2, Caffeine, biological studies 59-42-7, Phenylephrine 62-44-2, Phenacetin 76-57-3, Codeine 77-22-5, Caramiphen 77-23-6, Carbetapentane 90-82-4, Pseudoephedrine 101-40-6, Propylhexedrine 103-90-2, Acetaminophen 125-29-1, Hydrocodone 125-71-3, Dextromethorphan 526-36-3, Xylometazoline 835-31-4, Naphazoline 1309-42-8, Magnesium hydroxide 1491-59-4, Oxymetazoline 8050-81-5, Simethicone 14838-15-4, Phenylpropanolamine 15687-27-1, Ibuprofen 21645-51-2, Aluminum hydroxide, biological studies 22071-15-4, Ketoprofen 22204-53-1, Naproxen **33817-09-3** 56695-65-9, Rosaprostol 59122-46-2, Misoprostol 70667-26-4, Ornoprostil 73121-56-9, Enprostil 77287-05-9, Rioprostil 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 181695-72-7, Valdecoxib 198470-84-7, Parecoxib 202409-33-4, Etoricoxib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-administration agent; preparation of quinolinone prostaglandin E receptor ligands for treatment of pain, fever, inflammation, and other prostanoid mediated diseases)

IT **33817-09-3**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-administration agent; preparation of quinolinone prostaglandin E receptor ligands for treatment of pain, fever, inflammation, and other prostanoid mediated diseases)

RN 33817-09-3 CAPLUS
CN Benzeneethanamine, N,α-dimethyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:391513 CAPLUS
DOCUMENT NUMBER: 136:380122
TITLE: Methods and compositions for regulating memory consolidation
INVENTOR(S): Epstein, Mel H.; Wiig, Kjesten A.
PATENT ASSIGNEE(S): Sention, Inc., USA
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002039998	A2	20020523	WO 2001-US45793	20011031
WO 2002039998	A3	20040325		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2427388	A1	20020523	CA 2001-2427388	20011031
AU 200239464	A	20020527	AU 2002-39464	20011031
EP 1420768	A2	20040526	EP 2001-987226	20011031
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004534724	T	20041118	JP 2002-542373	20011031
AU 2002239464	B2	20070104	AU 2002-239464	20011031
EP 1743631	A2	20070117	EP 2006-20373	20011031
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR, AL, LT, LV, MK, RO, SI				
US 2003119884	A1	20030626	US 2002-139606	20020502
US 2003232890	A1	20031218	US 2003-444970	20030523
US 2005059743	A1	20050317	US 2004-791223	20040302
US 2006111448	A1	20060525	US 2005-133144	20050519
US 2006167111	A1	20060727	US 2005-303633	20051215
US 7244769	B2	20070717		
US 2006167112	A1	20060727	US 2005-305495	20051215
US 2007117869	A1	20070524	US 2006-557095	20060303
AU 2007201242	A1	20070419	AU 2007-201242	20070321

PRIORITY APPLN. INFO.:		
US 2000-245323P	P	20001101
EP 2001-987226	A3	20011031
US 2001-3740	A2	20011031
WO 2001-US145793	A	20011031
WO 2001-US45793	W	20011031
US 2002-139606	A2	20020502

US 2003-444970	A2	20030523
US 2003-473168P	P	20030523
US 2004-791223	A2	20040302
WO 2004-US15974	A2	20040521

OTHER SOURCE(S): MARPAT 136:380122

AB The present invention makes available methods and reagents for enhancing and/or restoring long-term memory function and performance, e.g., to improve long-term memory (LTM) and recall ability in animal subjects.

IT AIDS (disease)
(AIDS **dementia** complex; methods and compns. for enhancing memory consolidation)

IT Mental and behavioral disorders
(AIDS **dementia**; methods and compns. for enhancing memory consolidation)

IT Mental and behavioral disorders
(**dementia**; methods and compns. for enhancing memory consolidation)

IT Adrenoceptor agonists
Adrenoceptor agonists
Alzheimer's disease
Amnesia
Anti-**Alzheimer**'s agents
Anticonvulsants
Antidepressants
Antiparkinsonian agents
Antipsychotics
Anxiolytics
Cholinergic agonists
Cognition enhancers
Dopamine agonists
Epilepsy
Human
Learning
Learning disorders
Mammalia
Memory, biological
Mental retardation
Nervous system stimulants
Parkinson's disease
Permeation enhancers
Schizophrenia
(methods and compns. for enhancing memory consolidation)

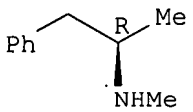
IT 113-45-1, Methylphenidate 300-62-9D, Amphetamine, derivs. 537-46-2 9061-61-4, Nerve growth factor **33817-09-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for enhancing memory consolidation)

IT **33817-09-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for enhancing memory consolidation)

RN 33817-09-3 CAPLUS

CN Benzeneethanamine, N,α-dimethyl-, (αR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L10 ANSWER 9 OF 13 MEDLINE on STN

ACCESSION NUMBER: 2005442439 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16110345
TITLE: Neuropharmacological, neuroprotective and amyloid precursor processing properties of selective MAO-B inhibitor antiparkinsonian drug, rasagiline.
AUTHOR: Youdim Moussa B H; Maruyama Wakako; Naoi Makato
CORPORATE SOURCE: Eve Topf and NPF Centers of Excellence for Neurodegenerative Diseases Research and Department of Pharmacology, Technion-Rappaport Faculty of Medicine, Haifa, Israel.. Youdim@tx.technion.ac.il
SOURCE: Drugs of today (Barcelona, Spain : 1998), (2005 Jun) Vol. 41, No. 6, pp. 369-91. Ref: 159
Journal code: 101160518. ISSN: 1699-3993.
PUB. COUNTRY: Spain
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200511
ENTRY DATE: Entered STN: 20 Aug 2005
Last Updated on STN: 8 Nov 2005
Entered Medline: 7 Nov 2005

AB Rasagiline (N-propargyl-1R-aminoindan) is a novel, highly potent, irreversible monoamine oxidase (MAO)-B inhibitor designed for use as an antiparkinsonian drug. Unlike selegiline, rasagiline is not derived from amphetamine or metabolized to neurotoxic **l-methamphetamine** derivative, and it does not have sympathomimetic activity. Moreover, at selective MAO-B inhibitory dosage, it does not induce a "cheese reaction." Rasagiline is effective as monotherapy or as an adjunct to L-dopa for patients with early and late Parkinson's disease. Adverse events do not occur with greater frequency in subjects receiving rasagiline than in those on placebo. Its S-isomer, TVP1022, is more than a thousand times less potent as an MAO inhibitor. However, both drugs have neuroprotective activities in neuronal cell cultures in response to various neurotoxins, as well as in vivo (e.g., in response to global ischemia, neurotrauma, head injury, anoxia, etc.), indicating that MAO inhibition is not a prerequisite for neuroprotection. The neuroprotective activity of these drugs has been demonstrated to be associated with the propargylamine moiety, which protects mitochondrial viability and mitochondrial permeability transition pore by activating Bcl-2 and downregulating the Bax family of proteins. Rasagiline processes amyloid precursor protein (APP) into the neuroprotective-neurotrophic soluble APPalpha (sAPPalpha) by protein kinase C- and mitogen-activated protein kinase-dependent activation of alpha-secretase, and increases nerve growth factor, glial cell- derived neurotrophic factor (GDNF) and brain-derived neurotrophic factor (BDNF) expression and proteins. Thus, rasagiline may induce neuroprotection, neuroplasticity and long-term potentiation. Rasagiline has therefore been chosen by the National Institutes of Health (NIH) to study its neuroprotective effects in neurodegenerative diseases. Long-term studies are required to evaluate the drug's disease-modifying prospects in Parkinson's and **Alzheimer**'s diseases.

AB Rasagiline (N-propargyl-1R-aminoindan) is a novel, highly potent, irreversible monoamine oxidase (MAO)-B inhibitor designed for use as an antiparkinsonian drug. Unlike selegiline, rasagiline is not derived from amphetamine or metabolized to neurotoxic **l-methamphetamine** derivative, and it does not have sympathomimetic activity. Moreover, at selective MAO-B inhibitory dosage, it does not induce a "cheese reaction." Rasagiline is effective as monotherapy or as an adjunct to L-dopa for patients with early and late Parkinson's disease. Adverse events do not occur with greater frequency in subjects receiving rasagiline than in those on placebo. Its S-isomer, TVP1022, is more than a thousand times less potent as an MAO inhibitor. However, both drugs

have neuroprotective activities in neuronal cell cultures in response to various neurotoxins, as well as in vivo (e.g., in response to global ischemia, neurotrauma, head injury, anoxia, etc.), indicating that MAO inhibition is not a prerequisite for neuroprotection. The neuroprotective activity of these drugs has been demonstrated to be associated with the propargylamine moiety, which protects mitochondrial viability and mitochondrial permeability transition pore by activating Bcl-2 and downregulating the Bax family of proteins. Rasagiline processes amyloid precursor protein (APP) into the neuroprotective-neurotrophic soluble APPalpha (sAPPalpha) by protein kinase C- and mitogen-activated protein kinase-dependent activation of alpha-secretase, and increases nerve growth factor, glial cell- derived neurotrophic factor (GDNF) and brain-derived neurotrophic factor (BDNF) expression and proteins. Thus, rasagiline may induce neuroprotection, neuroplasticity and long-term potentiation. Rasagiline has therefore been chosen by the National Institutes of Health (NIH) to study its neuroprotective effects in neurodegenerative diseases. Long-term studies are required to evaluate the drug's disease-modifying prospects in Parkinson's and **Alzheimer**'s diseases.

L10 ANSWER 10 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2004642924 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15573406
TITLE: Rasagiline: neurodegeneration, neuroprotection, and mitochondrial permeability transition.
AUTHOR: Youdim Moussa B H; Bar Am Orit; Yogev-Falach Merav; Weinreb Orly; Maruyama Wakako; Naoi Makato; Amit Tamar
CORPORATE SOURCE: Eve Topf and USA National Parkinson Foundation Centers of Excellence for Neurodegenerative Diseases Research and Department of Pharmacology, Technion-Faculty of Medicine, 31096 Haifa, Israel.. Youdim@tx.technion.ac.il
SOURCE: Journal of neuroscience research, (Jan 1-15 2005) Vol. 79, No. 1-2, pp. 172-9. Ref: 79
Journal code: 7600111. ISSN: 0360-4012.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 28 Dec 2004
Last Updated on STN: 19 Mar 2005
Entered Medline: 18 Mar 2005

AB Mitochondria are involved directly in cell survival and death. The assumption has been made that drugs that protect mitochondrial viability and prevent apoptotic cascade-induced mitochondrial permeability transition pore (MPTp) opening will be cytoprotective. Rasagiline (N-propargyl-1R-aminoindan) is a novel, highly potent irreversible monoamine oxidase (MAO) B inhibitor anti-Parkinson drug. Unlike selegiline, it is not derived from amphetamine, and is not metabolized to neurotoxic **L-methamphetamine** derivative. In addition, it does not have sympathomimetic activity. Rasagiline is effective as monotherapy or adjunct to levodopa for patients with early and late Parkinson's disease (PD) and adverse events do not occur with greater frequency in subjects receiving rasagiline than in those on placebo. Phase III controlled studies indicate that it might have a disease-modifying effect in PD that may be related to its neuroprotective activity. Its S isomer, TVP1022, is more than 1,000 times less potent as an MAO inhibitor. Both drugs, however, have neuroprotective activity in neuronal cell cultures in response to various neurotoxins, and in vivo in response to global ischemia, neurotrauma, head injury, anoxia, etc., indicating that MAO inhibition is not a prerequisite for neuroprotection. Their neuroprotective effect has been demonstrated to be associated

directly with the propargylamine moiety, which protects mitochondrial viability and MTPp by activating Bcl-2 and protein kinase C (PKC) and by downregulating the proapoptotic FAS and Bax protein families. Rasagiline and its derivatives also process amyloid precursor protein (APP) to the neuroprotective, neurotrophic, soluble APP alpha (sAPPalpha) by PKC- and MAP kinase-dependent activation of alpha-secretase. The identification of the propargylamine moiety as the neuroprotective component of rasagiline has led us to development of novel bifunctional anti-**Alzheimer** drugs (ladostigil) possessing cholinesterase and brain-selective MAO inhibitory activity and a similar neuroprotective mechanism of action. (c) 2004 Wiley-Liss, Inc.

AB Mitochondria are involved directly in cell survival and death. The assumption has been made that drugs that protect mitochondrial viability and prevent apoptotic cascade-induced mitochondrial permeability transition pore (MPTp) opening will be cytoprotective. Rasagiline (N-propargyl-1R-aminoindan) is a novel, highly potent irreversible monoamine oxidase (MAO) B inhibitor anti-Parkinson drug. Unlike selegiline, it is not derived from amphetamine, and is not metabolized to neurotoxic **L-methamphetamine** derivative. In addition, it does not have sympathomimetic activity. Rasagiline is effective as monotherapy or adjunct to levodopa for patients with early and late Parkinson's disease (PD) and adverse events do not occur with greater frequency in subjects receiving rasagiline than in those on placebo. Phase III controlled studies indicate that it might have a disease-modifying effect in PD that may be related to its neuroprotective activity. Its S isomer, TVP1022, is more than 1,000 times less potent as an MAO inhibitor. Both drugs, however, have neuroprotective activity in neuronal cell cultures in response to various neurotoxins, and in vivo in response to global ischemia, neurotrauma, head injury, anoxia, etc., indicating that MAO inhibition is not a prerequisite for neuroprotection. Their neuroprotective effect has been demonstrated to be associated directly with the propargylamine moiety, which protects mitochondrial viability and MTPp by activating Bcl-2 and protein kinase C (PKC) and by downregulating the proapoptotic FAS and Bax protein families. Rasagiline and its derivatives also process amyloid precursor protein (APP) to the neuroprotective, neurotrophic, soluble APP alpha (sAPPalpha) by PKC- and MAP kinase-dependent activation of alpha-secretase. The identification of the propargylamine moiety as the neuroprotective component of rasagiline has led us to development of novel bifunctional anti-**Alzheimer** drugs (ladostigil) possessing cholinesterase and brain-selective MAO inhibitory activity and a similar neuroprotective mechanism of action. (c) 2004 Wiley-Liss, Inc.

L10 ANSWER 11 OF 13 MEDLINE on STN

ACCESSION NUMBER:	90143749 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 2515726
TITLE:	Pharmacokinetics and metabolism of selegiline.
AUTHOR:	Heinonen E H; Myllyla V; Sotaniemi K; Lamintausta R; Salonen J S; Anttila M; Savijarvi M; Kotila M; Rinne U K
CORPORATE SOURCE:	Farmos Group Ltd, Research Center, Turku, Finland.
SOURCE:	Acta neurologica Scandinavica. Supplementum, (1989) Vol. 126, pp. 93-9. Journal code: 0370337. ISSN: 0065-1427.
PUB. COUNTRY:	Denmark
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	199003
ENTRY DATE:	Entered STN: 28 Mar 1990 Last Updated on STN: 6 Feb 1998 Entered Medline: 5 Mar 1990

AB Selegiline is readily absorbed from the gastrointestinal tract. It is distributed rapidly into the tissues, including the brain. It is the L-form of selegiline that is an active MAO-B inhibitor, the D-(+)-form

being 25 times less active. Selegiline is metabolised into L-(-)-desmethylselegiline (DES), L-(-)-amphetamine (A) and **L-(-)-methamphetamine** (MA), mainly in the liver. We measured the steady state concentrations of the metabolites in the serum and cerebrospinal fluid (CSF) of patients with Parkinson's or **Alzheimer**'s diseases who were on continuous selegiline therapy. The mean concentrations in serum and CSF were similar, and were not affected by the addition of levodopa. The mean concentrations of patients with **Alzheimer**'s or Parkinson's disease were 6.5 +/- 2.5 ng/ml for A, 14.7 +/- 6.5 ng/ml for MA and 0.9 +/- 0.7 ng/ml for DES. The metabolites of selegiline were excreted in urine, and the recovery as metabolites was 87%. Due to the stereospecificity and the low CSF concentrations of the (-)amphetamine metabolites during the therapy with 10 mg selegiline, these metabolites do not seem to contribute significantly to the clinical efficacy of selegiline.

AB Selegiline is readily absorbed from the gastrointestinal tract. It is distributed rapidly into the tissues, including the brain. It is the L-form of selegiline that is an active MAO-B inhibitor, the D-(+)-form being 25 times less active. Selegiline is metabolised into L-(-)-desmethylselegiline (DES), L-(-)-amphetamine (A) and **L-(-)-methamphetamine** (MA), mainly in the liver. We measured the steady state concentrations of the metabolites in the serum and cerebrospinal fluid (CSF) of patients with Parkinson's or **Alzheimer**'s diseases who were on continuous selegiline therapy. The mean concentrations in serum and CSF were similar, and were not affected by the addition of levodopa. The mean concentrations of patients with **Alzheimer**'s or Parkinson's disease were 6.5 +/- 2.5 ng/ml for A, 14.7 +/- 6.5 ng/ml for MA and 0.9 +/- 0.7 ng/ml for DES. The metabolites of selegiline were excreted in urine, and the recovery as metabolites was 87%. Due to the stereospecificity and the low CSF concentrations of the (-)amphetamine metabolites during the therapy with 10 mg selegiline, these metabolites do not seem to contribute significantly to the clinical efficacy of selegiline.

CT Check Tags: Female; Male
Aged
Alzheimer Disease: DT, drug therapy
Alzheimer Disease: ME, metabolism
Humans
Middle Aged
Parkinson Disease: DT, drug therapy
*Parkinson Disease: ME, metabolism
*Phenethylamines: ME, metabolism
*Phenethylamines: PK, pharmacokinetics
*Selegiline: ME, metabolism
*Selegiline: PK, pharmacokinetics
Selegiline: TU, therapeutic use

L10 ANSWER 12 OF 13 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:152187 BIOSIS
DOCUMENT NUMBER: PREV200500151361
TITLE: Rasagiline: Neurodegeneration, neuroprotection, and mitochondrial permeability transition.
AUTHOR(S): Youdim, Moussa B. H. [Reprint Author]; Bar Am, Orit; Yogev-Falach, Merav; Weinreb, Orly; Maruyama, Wakako; Naoi, Makato; Amit, Tamar
CORPORATE SOURCE: Fac MedDept Pharmacol, Technion Israel Inst Technol, POB 9697, IL-31096, Haifa, Israel
Youdim@tx.technion.ac.il
SOURCE: Journal of Neuroscience Research, (January 1 2005) Vol. 79, No. 1-2, pp. 172-179. print.
ISSN: 0360-4012 (ISSN print).
DOCUMENT TYPE: Article
General Review; (Literature Review)

LANGUAGE: English
ENTRY DATE: Entered STN: 20 Apr 2005
Last Updated on STN: 20 Apr 2005

AB Mitochondria are involved directly in cell survival and death. The assumption has been made that drugs that protect mitochondrial viability and prevent apoptotic cascade-induced mitochondrial permeability transition pore (MPTp) opening will be cytoprotective. Rasagiline (N-propargyl-1R-aminoindan) is a novel, highly potent irreversible monoamine oxidase (MAO) B inhibitor anti-Parkinson drug. Unlike selegiline, it is not derived from amphetamine, and is not metabolized to neurotoxic **L-methamphetamine** derivative. In addition, it does not have sympathomimetic activity. Rasagiline is effective as monotherapy or adjunct to levodopa for patients with early and late Parkinson's disease (PD) and adverse events do not occur with greater frequency in subjects receiving rasagiline than in those on placebo. Phase III controlled studies indicate that it might have a disease-modifying effect in PD that may be related to its neuroprotective activity. Its S isomer, TVP1022, is more than 1,000 times less potent as an MAO inhibitor. Both drugs, however, have neuroprotective activity in neuronal cell cultures in response to various neurotoxins, and in vivo in response to global ischemia, neurotrauma, head injury, anoxia, etc., indicating that MAO inhibition is not a prerequisite for neuro protection. Their neuroprotective effect has been demonstrated to be associated directly with the propargylamine moiety, which protects mitochondrial viability and MTPp by activating Bcl-2 and protein kinase C (PKC) and by downregulating the proapoptotic FAS and Bax protein families. Rasagiline and its derivatives also process amyloid precursor protein (APP) to the neuroprotective, neurotrophic, soluble APP a (sAPPalpha) by PKC- and MAP kinase-dependent activation of a-secretase. The identification of the propargylamine moiety as the neuroprotective component of rasagiline has led us to development of novel bifunctional anti-**Alzheimer** drugs (ladostigil) possessing cholinesterase and brain-selective MAO inhibitory activity and a similar neuroprotective mechanism of action. Copyright 2004 Wiley-Liss, Inc.

AB Mitochondria are involved directly in cell survival and death. The assumption has been made that drugs that protect mitochondrial viability and prevent apoptotic cascade-induced mitochondrial permeability transition pore (MPTp) opening will be cytoprotective. Rasagiline (N-propargyl-1R-aminoindan) is a novel, highly potent irreversible monoamine oxidase (MAO) B inhibitor anti-Parkinson drug. Unlike selegiline, it is not derived from amphetamine, and is not metabolized to neurotoxic **L-methamphetamine** derivative. In addition, it does not have sympathomimetic activity. Rasagiline is effective as monotherapy or adjunct to levodopa for patients with early and late Parkinson's disease (PD) and adverse events do not occur with greater frequency in subjects receiving rasagiline than in those on placebo. Phase III controlled studies indicate that it might have a disease-modifying effect in PD that may be related to its neuroprotective activity. Its S isomer, TVP1022, is more than 1,000 times less potent as an MAO inhibitor. Both drugs, however, have neuroprotective activity in neuronal cell cultures in response to various neurotoxins, and in vivo in response to global ischemia, neurotrauma, head injury, anoxia, etc., indicating that MAO inhibition is not a prerequisite for neuro protection. Their neuroprotective effect has been demonstrated to be associated directly with the propargylamine moiety, which protects mitochondrial viability and MTPp by activating Bcl-2 and protein kinase C (PKC) and by downregulating the proapoptotic FAS and Bax protein families. Rasagiline and its derivatives also process amyloid precursor protein (APP) to the neuroprotective, neurotrophic, soluble APP a (sAPPalpha) by PKC- and MAP kinase-dependent activation of a-secretase. The identification of the propargylamine moiety as the neuroprotective component of rasagiline has led us to development of novel bifunctional anti-**Alzheimer** drugs (ladostigil) possessing cholinesterase and brain-selective MAO inhibitory activity and a similar neuroprotective mechanism of action. Copyright

2004 Wiley-Liss, Inc.

L10 ANSWER 13 OF 13 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005036861 EMBASE
TITLE: Rasagiline: Neurodegeneration neuroprotection, and mitochondrial permeability transition.
AUTHOR: Youdim M.B.H.; Am O.B.; Yogev-Falach M.; Weinreb O.; Maruyama W.; Naoi M.; Amit T.
CORPORATE SOURCE: Prof. M.B.H. Youdim, Department of Pharmacology, Technion-Faculty of Medicine, PO Box 9697, 31096 Haifa, Israel. Youdim@tx.technion.ac.il
SOURCE: Journal of Neuroscience Research, (15 Jan 2005) Vol. 79, No. 1-2, pp. 172-179.
Refs: 77
ISSN: 0360-4012 CODEN: JNREDK
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 10 Feb 2005
Last Updated on STN: 10 Feb 2005

AB Mitochondria are involved directly in cell survival and death. The assumption has been made that drugs that protect mitochondrial viability and prevent apoptotic cascade-induced mitochondrial permeability transition pore (MPTp) opening will be cytoprotective. Rasagiline (N-propargyl-1R-aminoindan) is a novel, highly potent irreversible monoamine oxidase (MAO) B inhibitor anti-Parkinson drug. Unlike selegiline, it is not derived from amphetamine, and is not metabolized to neurotoxic **L-methamphetamine** derivative. In addition, it does not have sympathomimetic activity. Rasagiline is effective as monotherapy or adjunct to levodopa for patients with early and late Parkinson's disease (PD) and adverse events do not occur with greater frequency in subjects receiving rasagiline than in those on placebo. Phase III controlled studies indicate that it might have a disease-modifying effect in PD that may be related to its neuroprotective activity. Its S isomer, TVP1022, is more than 1,000 times less potent as an MAO inhibitor. Both drugs, however, have neuroprotective activity in neuronal cell cultures in response to various neurotoxins, and in vivo in response to global ischemia, neurotrauma, head injury, anoxia, etc., indicating that MAO inhibition is not a pre-requisite for neuroprotection. Their neuroprotective effect has been demonstrated to be associated directly with the propargylamine moiety, which protects mitochondrial viability and MTPp by activating Bcl-2 and protein kinase C (PKC) and by downregulating the pro-apoptotic FAS and Bax protein families. Rasagiline and its derivatives also process amyloid precursor protein (APP) to the neuroprotective, neurotrophic, soluble APP α (sAPPα) by PKC- and MAP kinase-dependent activation of α-secretase. The identification of the propargylamine moiety as the neuroprotective component of rasagiline has led us to development of novel bifunctional anti-**Alzheimer** drugs (ladostigil) possessing cholinesterase and brain-selective MAO inhibitory activity and a similar neuroprotective mechanism of action. .COPYRGT. 2004 Wiley-Liss, Inc.

AB Mitochondria are involved directly in cell survival and death. The assumption has been made that drugs that protect mitochondrial viability and prevent apoptotic cascade-induced mitochondrial permeability transition pore (MPTp) opening will be cytoprotective. Rasagiline (N-propargyl-1R-aminoindan) is a novel, highly potent irreversible monoamine oxidase (MAO) B inhibitor anti-Parkinson drug. Unlike selegiline, it is not derived from amphetamine, and is not metabolized to neurotoxic **L-methamphetamine** derivative. In addition, it does not have sympathomimetic activity. Rasagiline is effective as

PROCESSING COMPLETED FOR L26
L27 14 FOCUS L26 1-

=> d ibib abs hitstr 1-14

L27 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:774145 CAPLUS
DOCUMENT NUMBER: 134:289796
TITLE: (-)Deprenyl (selegiline): past, present and future
AUTHOR(S): Knoll, J.
CORPORATE SOURCE: Department of Pharmacology, Semmelweis University of Medicine, Budapest, H-1445, Hung.
SOURCE: Neurobiology (Budapest) (**2000**), 8(2), 179-199
CODEN: NROBEZ; ISSN: 1216-8068
PUBLISHER: Akademiai Kiado
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 52 refs. (-)Deprenyl (selegiline), the N-propargyl analog of (-)**methamphetamine**, is the only drug in clin. use which, by enhancing the impulse-propagation-mediated release of noradrenaline and dopamine in the brain (catecholaminergic activity enhancer, CAE), maintains (in small doses without side-effects) the brain catecholaminergic system on a higher activity level. (-)Deprenyl selectively stimulates the catecholaminergic neurons in the brain because, in contrast to phenethylamine and the **amphetamines**, which induce the continuous release of noradrenaline and dopamine from their intraneuronal stores; (-)deprenyl is devoid of this property. It is due to the CAE effect that: (a) the maintenance of rats on (-)deprenyl during the postdevelopmental phase of their life slows the age-related decline of sexual and learning performances and prolongs life significantly; (b) patients with early, untreated Parkinson's disease maintained on (-)deprenyl need levodopa later than their placebo-treated peers, and when on levodopa plus (-)deprenyl, they live significantly longer than patients on levodopa alone; and (c) in patients with moderately severe impairment from **Alzheimer**'s disease, treatment with (-)deprenyl slows the progression of the disease. It is reasonable to expect that a prophylactic low-dose administration of a safe CAE substance during the postdevelopmental phase of life will slow the age-related decline of behavioral performances, delay natural death and decrease susceptibility to Parkinson's disease and **Alzheimer**'s disease.
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1971:2625 CAPLUS
DOCUMENT NUMBER: 74:2625
ORIGINAL REFERENCE NO.: 74:431a,434a
TITLE: Psychotropic methoxyamphetamines: structure and activity in man
AUTHOR(S): Snyder, Solomon H.; Richelson, Elliott; Weingartner, Herbert; Faillace, Louis A.
CORPORATE SOURCE: Sch. of Med., Johns Hopkins Univ., Baltimore, MD, USA
SOURCE: Int. Symp. Amphetamines Relat. Compounds. Proc. (**1970**), Meeting Date 1969, 905-28. Editor(s): Costa, E. Raven Press: New York, N. Y.
CODEN: 17XKAB
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Mol. models of psychedelic drugs and factors that explain the similarity of their subjective effects were studied. 2,5-Dimethoxy-4-ethylamphetamine (I) produced significant subjective effects, such as a **mild** euphoria and enhanced self-awareness, in the complete absence of hallucinogenic or psychotomimetic effects. At 5-fold the minimal

monoamine oxidase (MAO) B inhibitor anti-Parkinson drug. Unlike selegiline, it is not derived from amphetamine, and is not metabolized to neurotoxic **L-methamphetamine** derivative In addition, it does not have sympathomimetic activity. Rasagiline is effective as monotherapy or adjunct to levodopa for patients with early and late Parkinson's disease (PD) and adverse events do not occur with greater frequency in subjects receiving rasagiline than in those on placebo. Phase III controlled studies indicate that it might have a disease-modifying effect in PD that may be related to its neuroprotective activity. Its S isomer, TVP1022, is more than 1,000 times less potent as an MAO inhibitor. Both drugs, however, have neuroprotective activity in neuronal cell cultures in response to various neurotoxins, and in vivo in response to global ischemia, neurotrauma, head injury, anoxia, etc., indicating that MAO inhibition is not a prerequisite for neuroprotection. Their neuroprotective effect was demonstrated to be associated directly with the propargylamine moiety, which protects mitochondrial viability and MTPp by activating Bcl-2 and protein kinase C (PKC) and by down-regulating the proapoptotic FAS and Bax protein families. Rasagiline and its derivs. also process amyloid precursor protein (APP) to the neuroprotective, neurotrophic, soluble APP α (sAPPα) by PKC- and MAP kinase-dependent activation of α-secretase. The identification of the propargylamine moiety as the neuroprotective component of rasagiline has led us to development of novel bifunctional anti-**Alzheimer** drugs (ladostigil) possessing cholinesterase and brain-selective MAO inhibitory activity and a similar neuroprotective mechanism of action.

AB A review. Mitochondria are involved directly in cell survival and death. The assumption was made that drugs that protect mitochondrial viability and prevent apoptotic cascade-induced mitochondrial permeability transition pore (MPTp) opening will be cytoprotective. Rasagiline (N-propargyl-1R-aminoindan) is a novel, highly potent irreversible monoamine oxidase (MAO) B inhibitor anti-Parkinson drug. Unlike selegiline, it is not derived from amphetamine, and is not metabolized to neurotoxic **L-methamphetamine** derivative In addition, it does not have sympathomimetic activity. Rasagiline is effective as monotherapy or adjunct to levodopa for patients with early and late Parkinson's disease (PD) and adverse events do not occur with greater frequency in subjects receiving rasagiline than in those on placebo. Phase III controlled studies indicate that it might have a disease-modifying effect in PD that may be related to its neuroprotective activity. Its S isomer, TVP1022, is more than 1,000 times less potent as an MAO inhibitor. Both drugs, however, have neuroprotective activity in neuronal cell cultures in response to various neurotoxins, and in vivo in response to global ischemia, neurotrauma, head injury, anoxia, etc., indicating that MAO inhibition is not a prerequisite for neuroprotection. Their neuroprotective effect was demonstrated to be associated directly with the propargylamine moiety, which protects mitochondrial viability and MTPp by activating Bcl-2 and protein kinase C (PKC) and by down-regulating the proapoptotic FAS and Bax protein families. Rasagiline and its derivs. also process amyloid precursor protein (APP) to the neuroprotective, neurotrophic, soluble APP α (sAPPα) by PKC- and MAP kinase-dependent activation of α-secretase. The identification of the propargylamine moiety as the neuroprotective component of rasagiline has led us to development of novel bifunctional anti-**Alzheimer** drugs (ladostigil) possessing cholinesterase and brain-selective MAO inhibitory activity and a similar neuroprotective mechanism of action.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:491224 CAPLUS
DOCUMENT NUMBER: 139:69162
TITLE: Preparation of quinolinones as prostaglandin E receptor ligands for treatment of pain, fever, inflammation, and other prostanoid receptor mediated

AU 2004251596	A1	20050106	AU 2004-251596		20040521
CA 2567746	A1	20050106	CA 2004-2567746		20040521
WO 2005000203	A2	20050106	WO 2004-US15974		20040521
WO 2005000203	A3	20051229			

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, US

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1635851	A2	20060322	EP 2004-752902		20040521

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

CN 1826105	A	20060830	CN 2004-80021116		20040521
JP 2007502863	T	20070215	JP 2006-533278		20040521
US 2006111448	A1	20060525	US 2005-133144		20050519
MX 2005PA12614	A	20060823	MX 2005-PA12614		20051122
US 2007117869	A1	20070524	US 2006-557095		20060303
US 2007099999	A1	20070503	US 2006-636644		20061208
US 2007100000	A1	20070503	US 2006-636702		20061208
US 2007197663	A1	20070823	US 2006-636703		20061208
PRIORITY APPLN. INFO.:			US 2000-245323P	P	20001101
			US 2001-3740	A2	20011031
			WO 2001-US45793	A	20011031
			US 2002-139606	A2	20020502
			US 2003-444970	A2	20030523
			EP 2001-987226	A3	20011031
			WO 2001-US145793	A	20011031
			US 2003-473168P	P	20030523
			US 2004-791223	A	20040302
			WO 2004-US15974	W	20040521
			US 2006-557095	A1	20060303

OTHER SOURCE(S): MARPAT 142:291427

AB **Mild cognitive** impairment and **Alzheimer**'s disease are treated with an amphetamine compound In one embodiment, the method includes administering an l-amphetamine compound In another embodiment, the method includes administering an l-methamphetamine compound

TI Methods for treating **mild cognitive** impairment and **Alzheimer**'s disease

AB **Mild cognitive** impairment and **Alzheimer**'s disease are treated with an amphetamine compound In one embodiment, the method includes administering an l-amphetamine compound In another embodiment, the method includes administering an l-methamphetamine compound

ST amphetamine methamphetamine mild cognition disorder **Alzheimer** disease therapy

IT **Alzheimer**'s disease
Analgesia
Analgesics
Anti-**Alzheimer**'s agents
Cognition enhancers
Cognitive disorders
(amphetamine for treating **mild cognitive** impairment and **Alzheimer**'s disease)

IT Behavior
(avoidance, inhibitory; amphetamine for treating **mild cognitive** impairment and **Alzheimer**'s disease)

IT Memory, biological
(consolidation, procedural, declarative; amphetamine for treating **mild cognitive** impairment and **Alzheimer**'s

monotherapy or adjunct to levodopa for patients with early and late Parkinson's disease (PD) and adverse events do not occur with greater frequency in subjects receiving rasagiline than in those on placebo. Phase III controlled studies indicate that it might have a disease-modifying effect in PD that may be related to its neuroprotective activity. Its S isomer, TVP1022, is more than 1,000 times less potent as an MAO inhibitor. Both drugs, however, have neuroprotective activity in neuronal cell cultures in response to various neurotoxins, and in vivo in response to global ischemia, neurotrauma, head injury, anoxia, etc., indicating that MAO inhibition is not a pre-requisite for neuroprotection. Their neuroprotective effect has been demonstrated to be associated directly with the propargylamine moiety, which protects mitochondrial viability and MTPp by activating Bcl-2 and protein kinase C (PKC) and by downregulating the pro-apoptotic FAS and Bax protein families. Rasagiline and its derivatives also process amyloid precursor protein (APP) to the neuroprotective, neurotrophic, soluble APP α (sAPPα) by PKC- and MAP kinase-dependent activation of α-secretase. The identification of the propargylamine moiety as the neuroprotective component of rasagiline has led us to development of novel bifunctional anti-**Alzheimer** drugs (ladostigil) possessing cholinesterase and brain-selective MAO inhibitory activity and a similar neuroprotective mechanism of action. .COPYRGT. 2004 Wiley-Liss, Inc.

```
=> d his

     (FILE 'HOME' ENTERED AT 16:08:31 ON 08 NOV 2007)

     FILE 'REGISTRY' ENTERED AT 16:08:51 ON 08 NOV 2007
L1           503 S AMPHETAMINE
L2             3 S AMPHETAMINE AND AMFETAMINE
L3             3 S METAMFETAMINE AND METHAMPHETAMINE
L4             1 S AMPHETAMINE AND LEVO

     FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE' ENTERED AT 16:12:00 ON 08 NOV 2007
L5        338080 S ALZHEIMER OR DEMENTIA OR (SENILE (L) DEMENTIA) OR ALZHEIMER?
L6        346406 S L5 OR ((MILD (L) COGNITIVE) OR FORGETFULNESS)
L7           734 S L6 AND (300-62-9/RN OR AMPHETAMINE OR AMFETAMINE OR METHYLPH
L8            18 S L6 AND (156-34-3/RN OR LEVOAMPHETAMINE OR L-AMPHETAMINE OR L
L9           259 S L6 AND (METHAMPHETAMINE OR METHYLAMPHETAMINE OR DEOXYEPHEDRI
L10           13 S L6 AND (33817-09-3/RN OR LEVMETAMFETAMINE OR L-METHYLAMPHETA
L11           85 S L7 AND L9
L12            4 S L8 AND L10
L13           25 S L11 AND PD <=2001
L14           22 S L11 AND PD <=2000
L15        83146 S EPSTEIN OR WIIG OR VERHEIJEN
L16            0 S L15 AND L11
L17           10 S EPSTEIN/AU OR WIIG/AU OR VERHEIJEN/AU
L18            0 S L17 AND L11
L19            0 S L17 AND (L7 OR L9)
L20            0 S EPSTEIN/IV OR WIIG/IV OR VERHEIJEN/IV
L21            0 S EPSTEIN/AS OR WIIG/AS OR VERHEIJEN/AS
L22            0 S L17 AND ALZHEIMER?
L23           83 S L15 AND (ALZHEIMER?)
L24            0 S L23 AND (L7 OR L9)

=> s l13 or l14
L25           25 L13 OR L14

=> dup rem l25
PROCESSING COMPLETED FOR L25
L26           14 DUP REM L25 (11 DUPLICATES REMOVED)

=> focus
```

that the increase of the DA transporters was not sufficient for complete function recovery. These findings have treatment implications because they suggest that protracted abstinence may reverse some of **methamphetamine**-induced alterations in brain DA terminals.

L27 ANSWER 4 OF 14 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2000014440 EMBASE
TITLE: [EEG in psychiatry].
EEG IN DER PSYCHIATRIE.
AUTHOR: Saletu B.; Anderer P.
CORPORATE SOURCE: Dr. B. Saletu, Bereich Schlafforsch./Pharmakopsych., Universitatsklinik fur Psychiatrie, Wahringer Gurtel 18-20, A-1090 Wien, Austria
SOURCE: Neuropsychiatrie, (**1999**) Vol. 13, No. 4, pp. 161-177.
Refs: 60
ISSN: 0948-6259 CODEN: NUROF9
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
032 Psychiatry
037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: English; German
ENTRY DATE: Entered STN: 20 Jan 2000
Last Updated on STN: 20 Jan 2000

AB Since the development of the EEG by Hans Berger in 1929 there has been increasing evidence that mental disorders are caused by aberrant electrophysiological brain function. Findings were initially based on visual, later on computer-assisted quantitative analyses. This article gives an overview of sources and registration techniques of normal and abnormal brain waves and provides an insight into quantitative EEG analysis and EEG mapping. It includes a description of EEG findings in the most important mental disorders such as schizophrenia with predominantly negative and positive symptomatology, major depression, generalized anxiety disorder, agoraphobia, obsessive compulsive disorder, multiinfarct **dementia**, **dementia** of the **Alzheimer** type and alcohol dependence. Moreover, EEG changes after the major representative drugs of the main psychopharmacological classes such as neuroleptics, antidepressants, anxiolytic sedatives, psychostimulants and nootropics are described. It is interesting that the EEG changes in mental disorders are opposite to those induced by the psychotropic drugs indicated for the treatment of the former. By means of pharmaco EEG one may determine if, how, when and at which dosage a drug acts on the target organ - the human brain. Based on multiple-channel recordings of the EEG and of event-related potentials with subsequent neuroimaging in 2 dimensions (mapping) and 3 dimensions (EEG-CT: LORETA = low resolution electromagnetic tomography) it seems possible to show differences in brain function between an individual patient and normal controls (e.g. Z-values = number of standard deviations from the norm), which is the basis for neurophysiological classification of psychiatric disorders and thus makes it possible to choose the optimum drug treatment. Thus, the EEG may represent a valuable objective and quantitative instrument in the diagnosis and treatment of mental disorders.

L27 ANSWER 5 OF 14 MEDLINE on STN

ACCESSION NUMBER: 2001475668 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11519485
TITLE: Acceleration of HIV **dementia** with **methamphetamine** and cocaine.
AUTHOR: Nath A; Maragos W F; Avison M J; Schmitt F A; Berger J R
CORPORATE SOURCE: Department of Neurology, University of Kentucky, Lexington

40526-0284, USA.
SOURCE: Journal of neurovirology, **(2001 Feb)** Vol. 7, No. 1, pp. 66-71.
Journal code: 9508123. ISSN: 1355-0284.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 27 Aug 2001
Last Updated on STN: 24 Sep 2001
Entered Medline: 20 Sep 2001

AB We report a patient with rapidly accelerating HIV **dementia** accompanied by seizures and an unusual movement disorder despite highly potent antiretroviral therapy. This clinical constellation was associated with the non-parenteral use of **methamphetamine** and cocaine. Fractional enhancement time on post contrast magnetic resonance imaging studies revealed a progressive breakdown of the blood brain barrier particularly in the basal ganglia. The movement disorder but not the **dementia** responded to a combination of dopamine replacement and anticholinergic therapy. While the movement disorder may have been unmasked by concomitant anticonvulsant therapy, we suggest in this instance, that prior drug abuse synergized with HIV to cause a domino effect on cerebral function. Careful attention and analysis to histories of remote non-injecting drug abuse may help substantiate our hypothesis.

L27 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:543306 CAPLUS
DOCUMENT NUMBER: 117:143306
TITLE: The pharmacology of 1-phenyl-2-propylaminopentane (PPAP), a deprenyl-derived new spectrum psychostimulant
AUTHOR(S): Knoll, J.; Knoll, B.; Torok, Z.; Timar, J.; Yasar, S.
CORPORATE SOURCE: Dep. Pharmacol., Semmelweis Univ. Med., Budapest, H-1445, Hung.
SOURCE: Archives Internationales de Pharmacodynamie et de Therapie (**1992**), 316, 5-29
CODEN: AIPTAK; ISSN: 0003-9780
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The peculiar tyramine uptake inhibitory effect of (-)deprenyl prompted structure-activity relationship studies aiming to develop new spectrum central nervous system stimulants which are devoid of MAO inhibitory potency and operate de facto as indirectly acting, nonreleasing sympathomimetics. Of the derivs. synthesized for this purpose, 1-phenyl-2-propylaminopentane (PPAP) was selected and its pharmacol. spectrum is presented. PPAP is taken up by the catecholamine axon terminal membrane and the vesicular membrane but it is devoid of catecholamine-releasing property. As a result, PPAP is, by inference, a potent inhibitor of the uptake of indirectly acting sympathomimetic releasers and of the catecholamine transmitters. This was proved, on the one hand, by measuring the uptake of [14C]PPAP into the catecholaminergic axon terminals and the inhibition of the uptake of [3H]noradrenaline and [3H]dopamine by PPAP in the rat brain, and, on the other hand, on the pulmonary artery strip of the rabbit and, in vivo, using the rat nictitating membrane as a detector. PPAP increases motility at 2 mg/kg and, in contrast to **amphetamine**, inhibits it at very high doses (50 mg/kg) only. A two-sided antagonism in the motility-increasing effect between PPAP and **amphetamine** and, more pronounced, between PPAP and mazindol was detected. PPAP is substantially less effective in inducing stereotyped behavior than either **amphetamine** or **methamphetamine**. PPAP facilitates learning and retention, is

highly potent in antagonizing the tetrabenazine-induced depression in behavioral tests and is very effective in the forced swimming test. Whereas **amphetamines** facilitate performance in a very narrow range of low doses, which turns, at a modest elevation of the dose, into the opposite effect, PPAP improves performance within a reasonably broad dose range. Based on the peculiar pharmacol. profile of PPAP, it appears to be potentially useful for the treatment of depression, **Alzheimer**'s disease and attention-deficit-hyperkinetic disorder.

L27 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:701656 CAPLUS
DOCUMENT NUMBER: 123:132666
TITLE: Anticonvulsant and antiepileptogenic effect of L-deprenyl (selegiline) in the kindling model of epilepsy
AUTHOR(S): Loescher, Wolfgang; Hoenack, Dagmar
CORPORATE SOURCE: Dep. Pharmacol., Sch. Vet. Med., Hannover, Germany
SOURCE: Journal of Pharmacology and Experimental Therapeutics (**1995**), 274(1), 307-14
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB L-Deprenyl (selegiline) is an irreversible inhibitor of monoamine oxidase type B, but also exerts several effects on dopamine and noradrenaline systems independent of monoamine oxidase type B inhibition. Thanks to these properties, L-deprenyl has gained wide acceptance in the therapy of Parkinson's disease by using L-deprenyl both with levodopa and alone. Furthermore, L-deprenyl improves the performance of patients with **Alzheimer**'s disease. Epilepsy, particularly temporal lobe epilepsy with complex-partial seizures, is often associated with disturbances of cognitive function and behavior, and it has been suggested that a drug combining cognition-enhancing and antiepileptic activity would be of benefit in the treatment of epileptic patients. This prompted us to study if L-deprenyl exerts anticonvulsant efficacy in amygdala-kindled rats, i.e., a useful model of complex-partial seizures in humans. In addition to anticonvulsant activity, i.e., effects on already developed seizures, we determined whether L-deprenyl exhibits antiepileptogenic properties, i.e., suppressive effects on development of kindling. In all expts., behavior alterations of the rats in response to L-deprenyl were monitored closely. In order to assess the role of active metabolites in the anticonvulsant and behavioral effects of L-deprenyl in the kindling model, the D-enantiomer of deprenyl, which is metabolized to more potent compds. (D-**amphetamine** and D-**methamphetamine**) than the L-enantiomer, was used for comparison. In fully kindled rats, L-deprenyl potently increased the threshold for focal afterdischarges. The most marked increase in afterdischarge threshold (up to 250% above control) was seen after a dose of 10 mg/kg, whereas the D-enantiomer was ineffective at this dosage. In contrast to the lack of anticonvulsant activity, D-deprenyl was more potent than L-deprenyl to induce **amphetamine**-like behavioral adverse effects such as stereotypies, thus indicating that degradation to active metabolites is involved in the behavioral but not anticonvulsant effects of deprenyl. This was substantiated by the observation that increase of dosage of L-deprenyl to 20 or 40 mg/kg induced marked **amphetamine**-like adverse effects, whereas the anticonvulsant effect was reduced compared to lower doses. Chronic treatment with L-deprenyl during kindling acquisition did not prevent kindling, but significantly retarded the development of some kindling parameters. The present study is the first to demonstrate potent anticonvulsant effects of L-deprenyl. In view of the neuroprotective and cognition-enhancing effects of this drug, L-deprenyl might be of clin. benefit in patients with epilepsy.

L27 ANSWER 8 OF 14 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights

TITLE: (-)Deprenyl (selegiline), a catecholaminergic activity enhancer (CAE) substance acting in the brain
AUTHOR(S): Knoll, Joseph
CORPORATE SOURCE: Department of Pharmacology, Semmelweis University of Medicine, Budapest, H-1445, Hung.
SOURCE: Pharmacology & Toxicology (Copenhagen) (**1998**), 82(2), 57-66
CODEN: PHTOEH; ISSN: 0901-9928
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 90 refs. β-Phenylethylamine and its long acting derivs., the **amphetamines**, are mixed-acting stimulants of the sympathetic system in the brain. They enhance the impulse propagation mediated release of catecholamines (catecholaminergic activity enhancer effect) and displace catecholamines from their stores (catecholamine releasing effect). (-)Deprenyl (selegiline), a close structural relative to (-)**methamphetamine**, is the first catecholaminergic activity enhancer substance in clin. use devoid of catecholamine releasing property, being therefore free of the "cheese effect" and of the dependence capacity of the **amphetamines**. (-)Deprenyl is also a highly potent and selective, irreversible inhibitor of monoamine oxidase type B. (-)Deprenyl enhances superoxide dismutase and catalase activity in the striatum, protects the nigrostriatal dopaminergic neurons against selective neurotoxins (6-hydroxy-dopamine, MPTP, 4-N-(2-chloroethyl)-N-ethyl-2-bromobenzylamine) and prevents characteristic age-related morphol. changes in the neurocytes of the substantia nigra. Maintenance of rats on (-)deprenyl during the post-developmental phase of their life slows the age-related decline of sexual and learning performances and prolongs life significantly. Patients with early, untreated Parkinson's disease maintained on (-)deprenyl need levodopa significantly later than their placebo-treated peers, and when on levodopa plus (-)deprenyl, they live significantly longer than patients on levodopa alone. In patients with moderately severe impairment from **Alzheimer**'s disease, treatment with (-)deprenyl slows the progression of the disease. It may be supposed that a prophylactic low dose administration of a safe catecholaminergic activity enhancer substance during the post-developmental phase of life will slow the age-related decline of behavioral performances, delay natural death and decrease susceptibility to Parkinson's disease and **Alzheimer**'s disease.

REFERENCE COUNT: 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 10 OF 14 MEDLINE on STN
ACCESSION NUMBER: 90143749 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2515726
TITLE: Pharmacokinetics and metabolism of selegiline.
AUTHOR: Heinonen E H; Myllyla V; Sotaniemi K; Lamintausta R; Salonen J S; Anttila M; Savijarvi M; Kotila M; Rinne U K
CORPORATE SOURCE: Farmos Group Ltd, Research Center, Turku, Finland.
SOURCE: Acta neurologica Scandinavica. Supplementum, **(1989)** Vol. 126, pp. 93-9.
Journal code: 0370337. ISSN: 0065-1427.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199003
ENTRY DATE: Entered STN: 28 Mar 1990
Last Updated on STN: 6 Feb 1998
Entered Medline: 5 Mar 1990

AB Selegiline is readily absorbed from the gastrointestinal tract. It is distributed rapidly into the tissues, including the brain. It is the L-form of selegiline that is an active MAO-B inhibitor, the D-(+)-form

reserved on STN
ACCESSION NUMBER: 1995138892 EMBASE
TITLE: Aliphatic propargylamines, a new series of potent selective, irreversible non-**amphetamine**-like MAO-B inhibitors: Their structures, function and pharmacological implications.
AUTHOR: Yu P.H.; Davis B.A.; Boulton A.A.
CORPORATE SOURCE: P.H. Yu, Neuropsychiatric Research Unit, Department of Psychiatry, University of Saskatchewan, Saskatoon, Sask., Canada
SOURCE: Advances in Experimental Medicine and Biology, (**1995**) Vol. 363, pp. 17-23.
ISSN: 0065-2598 CODEN: AEMBAP
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 31 May 1995
Last Updated on STN: 31 May 1995

AB 1-Deprenyl, a selective irreversible MAO-B inhibitor, has been shown to prolong the onset of disability in Parkinson's patients and to improve cognitive behavior in **Alzheimer**'s disease. It has been claimed that 1- deprenyl exhibits neuroprotective and neurorescue effects in several animal models. The precise mechanism of these effects is unknown. It is yet to be established whether or not the effects are unique to 1-deprenyl; a drug which possesses, in addition to inhibition of MAO-B activity, an **amphetamine** moiety. Based on the fact that several N-methylpropargylamine derivatives have been shown to be MAO inhibitors and that aliphatic amines are typical MAO-B substrates with a high affinity for the enzyme, we have synthesized a series of aliphatic propargylamines which have turned out to be highly potent, selective and irreversible MAO-B inhibitors, structurally unrelated to **amphetamine**. The potency of these inhibitors is related to their chain length and the substitution of a hydrogen on the terminal carbon of the aliphatic chain. MAO-I activity, as assessed in vitro, increased as the aliphatic carbon chain length increased; substitution of the hydrogen at the aliphatic chain terminal by hydroxyl, carboxyl or carboethoxyl groups or replacement of the methyl group on the nitrogen atom by an ethyl group considerably reduced their inhibitory activity. Stereospecific effects were observed with the R-(-)-enantiomer being 20-fold more active than the S-(+)- enantiomer. Inhibitors with relatively short carbon chain lengths (i.e. four to six carbons) were found to be more potent at inhibiting brain MAO-B activity in vivo especially after oral administration. M-2-PP [N-methyl-N- (2-pentyl)-propargylamine] and 2-HxMP [N-(2-hexyl)-N-methyl-propargylamine], for example, are approximately 5 fold more potent and selective inhibitors of mouse brain MAO-B activity than 1-deprenyl after oral administration. Like 1- deprenyl, chronic low dose administration of the aliphatic propargylamines caused a slight cumulative inhibition of MAO-A activity in the mouse brain. These new inhibitors selectively inhibited MAO-B activity in vivo, i.e. they increased 2-phenylethylamine levels substantially, but did not affect the levels of dopamine, DOPAC, HVA, 5-HT and 5-HIAA. Both 2-HxMP and M-2-PP have been shown to be capable of protecting against MPTP-induced nigrostriatal dopamine depletion and against DSP-4 [N-(2-chloroethyl)-N-ethyl-2- bromobenzylamine] induced noradrenaline depletion in the hippocampus of the mouse. These new aliphatic MAO-B inhibitors seem to be nontoxic and may be useful in the treatment of certain neuropsychiatric disorders.

L27 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:70640 CAPLUS
DOCUMENT NUMBER: 128:212439

perceptible dose of LSD (lysergic acid diethylamide) or other psychedelic drugs, marked hallucinogenic and psychotomimetic changes were usually observed Although 2,5-dimethoxy-4-**methylamphetamine** (DOM) has been shown to be hallucinogenic and psychotomimetic, in low doses, its subjective effects were similar to those of I. The ability of I to produce **mild** euphoria and enhanced self-awareness in the absence of **cognitive** or perceptual distortion suggests that if may be of therapeutic utility in psychiatry.

L27 ANSWER 3 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2001676629 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11717374
TITLE: Loss of dopamine transporters in **methamphetamine** abusers recovers with protracted abstinence.
AUTHOR: Volkow N D; Chang L; Wang G J; Fowler J S; Franceschi D; Sedler M; Gatley S J; Miller E; Hitzemann R; Ding Y S; Logan J
CORPORATE SOURCE: Medical and Chemistry Departments, Brookhaven National Laboratory, Upton, New York 11973, USA.. volkow@bnl.gov
CONTRACT NUMBER: DA00280 (NIDA)
DA06891 (NIDA)
DA7092-01 (NIDA)
MO1 RR10710 (NCRR)
MO1RR 00425 (NCRR)
SOURCE: The Journal of neuroscience : the official journal of the Society for Neuroscience, **(2001 Dec 1)** Vol. 21, No. 23, pp. 9414-8.
Journal code: 8102140. E-ISSN: 1529-2401.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 28 Nov 2001
Last Updated on STN: 25 Jan 2002
Entered Medline: 11 Jan 2002

AB **Methamphetamine** is a popular drug of abuse that is neurotoxic to dopamine (DA) terminals when administered to laboratory animals. Studies in **methamphetamine** abusers have also documented significant **loss** of DA transporters (used as markers of the DA terminal) that are associated with slower motor function and decreased **memory**. The extent to which the loss of DA transporters predisposes **methamphetamine** abusers to neurodegenerative disorders such as Parkinsonism is unclear and may depend in part on the degree of recovery. Here we assessed the effects of protracted abstinence on the loss of DA transporters in striatum, in **methamphetamine** abusers using positron emission tomography and [(11)C]d-threo-methylphenidate (DA transporter radioligand). Brain DA transporters in five **methamphetamine** abusers evaluated during short abstinence (<6 months) and then retested during protracted abstinence (12-17 months) showed significant increases with protracted abstinence (caudate, +19%; putamen, +16%). Although performance in some of the tests for which we observed an association with DA transporters showed some improvement, this effect was not significant. The DA transporter increases with abstinence could indicate that **methamphetamine**-induced DA transporter loss reflects temporary adaptive changes (i.e., downregulation), that the loss reflects DA terminal damage but that terminals can recover, or that remaining viable terminals increase synaptic arborization. Because neuropsychological tests did not improve to the same extent, this suggests

being 25 times less active. Selegiline is metabolised into L-(-)-desmethylselegiline (DES), L-(-)-**amphetamine** (A) and L-(-)-**methamphetamine** (MA), mainly in the liver. We measured the steady state concentrations of the metabolites in the serum and cerebrospinal fluid (CSF) of patients with Parkinson's or **Alzheimer**'s diseases who were on continuous selegiline therapy. The mean concentrations in serum and CSF were similar, and were not affected by the addition of levodopa. The mean concentrations of patients with **Alzheimer**'s or Parkinson's disease were 6.5 +/- 2.5 ng/ml for A, 14.7 +/- 6.5 ng/ml for MA and 0.9 +/- 0.7 ng/ml for DES. The metabolites of selegiline were excreted in urine, and the recovery as metabolites was 87%. Due to the stereospecificity and the low CSF concentrations of the (-)**amphetamine** metabolites during the therapy with 10 mg selegiline, these metabolites do not seem to contribute significantly to the clinical efficacy of selegiline.

L27 ANSWER 11 OF 14 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1993:309774 BIOSIS
DOCUMENT NUMBER: PREV199345016299
TITLE: The interactions of MK-801 with the analogues **amphetamine** D-**methamphetamine**, D-MDMA or D-fenfluramine: Neural damage and neural protection.
AUTHOR(S): Miller, Diane B.; O'Callaghan, James P.
CORPORATE SOURCE: U.S. EPA, Health Effects Res. Lab., RTP, NC 27711, USA
SOURCE: Neurotoxicology (Little Rock), (**1992**) Vol. 13, No. 4, pp. 875.
Meeting Info.: Tenth International Neurotoxicology Conference on Mechanisms of Developmental Neurotoxicology. Little Rock, Arkansas, USA. September 28-October 1, 1992.
CODEN: NRTXDN. ISSN: 0161-813X.
DOCUMENT TYPE: Conference; (Meeting)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jun 1993
Last Updated on STN: 3 Jan 1995

L27 ANSWER 12 OF 14 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1982130272 EMBASE
TITLE: Clonidine: New research in psychotropic drug pharmacology.
AUTHOR: Fielding S.; Lal H.
CORPORATE SOURCE: Hoechst-Roussel Pharmaceut. Inc., Somerville, NJ 08876, United States
SOURCE: Medicinal Research Reviews, (**1981**) Vol. 1, No. 1, pp. 97-123.
ISSN: 0198-6325 CODEN: MRREDD
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
032 Psychiatry
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Dec 1991
Last Updated on STN: 9 Dec 1991

AB Clonidine has been studied extensively with respect to its centrally mediated antihypertensive actions. Those actions of the clonidine that may be of interest in psychiatry, neurology, and behavioral pharmacology have not as yet been thoroughly investigated. It is only recently that central α(2)-receptors have been implicated in a number of physiological functions which are associated with a number of disease processes. Depression, schizophrenia, **dementia**, heroin and alcohol withdrawal, and anxiety are some examples. Because of clonidine's specificity and potency in stimulating α(2)-receptors in the brain, numerous possibilities exist to use this drug as a tool to help ascertain

the pathogenesis of many psychiatric illnesses as well as to investigate avenues for development of new psychotropic drugs. It is this aspect of clonidine's action that prompted the authors to prepare this review.

L27 ANSWER 13 OF 14 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2001387448 EMBASE
TITLE: Application of genomics to drug design: The example of the histamine H(3) receptor.
AUTHOR: Schwartz J.C.; Morisset S.; Rouleau A.; Tardivel-Lacombe J.; Gbahou F.; Ligneau X.; Heron A.; Sasse A.; Stark H.; Schunack W.; Ganellin R.C.; Arrang J.M.
CORPORATE SOURCE: J.-C. Schwartz, Unite de Neurobiologie, INSERM, Centre Paul Broca, 2 Rue Alesia, 75014 Paris, France. schwartz@broca.inserm.fr
SOURCE: European Neuropsychopharmacology, (**2001**) Vol. 11, No. 6, pp. 441-448.
Refs: 31
ISSN: 0924-977X CODEN: EURNE8
PUBLISHER IDENT.: S 0924-977X(01)00121-3
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
030 Clinical and Experimental Pharmacology
032 Psychiatry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 26 Nov 2001
Last Updated on STN: 26 Nov 2001

AB The histamine H(3) receptor was characterized in the 1980s as an autoreceptor regulating histamine release in brain. Since then, selective drugs have been designed, many of them displaying a high potency in vivo, and used in many studies to delineate the implications of cerebral histaminergic systems in physiological functions such as arousal or cognitive functions. The recent cloning of the H(3) receptor, more than 15 years later, has allowed to start molecular studies that led to important findings for optimization of drug design. In agreement some ligands display distinct affinities for the recombinant rat and human H(3) receptors, a difference that we assign to two amino acids in the third transmembrane domain. In addition, H(3) autoreceptors present in the brain display high constitutive activity including in vivo. As a consequence, inverse agonists enhance histamine neuron activity and constitute a novel potential therapeutic approach to schizophrenia and **Alzheimer**'s disease. Copyright .COPYRGT. 2001 Elsevier Science B.V.

L27 ANSWER 14 OF 14 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1995018273 EMBASE
TITLE: Introduction: Examination of clinical and preclinical pharmacologic data relating to abuse liability of l-deprenyl (selegiline).
AUTHOR: Goldberg S.R.; Yasar S.; Bergman J.; Youdim M.B.H.
CORPORATE SOURCE: Dr. S.R. Goldberg, Intramural Research Program, National Institute on Drug Abuse, P.O. Box 5180, 4940 Eastern Avenue, Baltimore, MD 21224, United States
SOURCE: Clinical Pharmacology and Therapeutics, (**1994**) Vol. 56, No. 6 II SUPPL., pp. 721-724.
ISSN: 0009-9236 CODEN: CLPTAT
COUNTRY: United States
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index

	038	Adverse Reactions Titles
	040	Drug Dependence, Alcohol Abuse and Alcoholism
	008	Neurology and Neurosurgery
LANGUAGE:	English	
ENTRY DATE:	Entered STN: 9 Feb 1995	
	Last Updated on STN: 9 Feb 1995	

=>